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No. 3—The Immunology and Epidemiology of Some Virus Diseases *

By

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There was again a crowded attendance at the session of Congress devoted to the consideration of Mr. Crawford's paper, which was held in the College Hall of the Royal (Dick) Veterinary College, on Wednesday, July 30th, 1947, under the chairmanship of Professor D. C. Matheson, M.R.C.V.S., D.V.S.M., F.R.S.E.

The CHAIRMAN said that the paper had been circulated and would be taken as read. Mr. Crawford did not wish to add anything to it. He had to express Dr. Galloway's apologies and regrets that he was not able to be present to open the discussion, as indicated on the agenda, but it had been possible to fill his place at very short notice by Dr. W. M. Henderson (Pirbright).

Following is the text of Mr. Crawford's paper.

The Immunology and Epidemiology of Some Virus Diseases

An infectious disease is essentially a manifestation of a host-parasite relationship and such a relationship is not a static condition but one capable of continual change. Theoretically the ideal relationship is an equilibrium or symbiosis; when the parasite and its host have attained a state of perfect equilibrium disease is not manifested, the host is infected by the parasite without any apparent ill-effect being produced. Where disease results from the infection the adaptation of one to the other has not yet attained perfection. The state of adaptation will obviously vary with the length of time during which the parasite has been associated with any particular host, and the effect produced by a parasite when it attacks a new host may be very different from that produced in its true or definite host.

The successful parasite must have perfected some means of penetration into its host. Having done so, it must be able to reach the particular tissues which are favourable to its development and it must also have some means whereby it can pass from one host to another. The reactions of the host vary; it may endeavour to prevent the parasite penetrating, to destroy it after penetration, or, if it cannot destroy it, to neutralize any ill-effects which it may cause.

In these activities both the parasite and the host are influenced by the environmental conditions in which both live.

In this consideration of one or two of the many aspects of immunity and epidemiology of certain virus diseases, I shall endeavour to look upon the diseases not only with the eye of the pathologist or the clinician, but also with that of the biologist when he studies a host-parasite relationship.

In doing so, I know that I am begging the question as to whether the viruses are actually living parasites or not. I am not going to attempt to discuss that most intriguing and difficult question. I shall content myself by saying that in their power of multiplying, in their nutritional requirements and their reactions to heat and to disinfecting agents, the viruses possess sufficient of the attributes of living parasites to justify their being considered as such in the present state of our knowledge. I shall consider them as resembling very closely minute bacteria from which they differ chiefly by their smaller size and by the important feature that, so far as we know, they are compulsory intra-cellular parasites which cannot multiply in a cell-free medium.

Immunity

To come now to immunity against virus diseases: A feature of many virus diseases is the solid and lasting immunity which is developed by the host as a result of natural infection. That is not true of all virus infections but it is a feature of many. Influenza and the common cold are examples in which immunity is not durable. Until recently herpes in man would have been cited as an example of a disease from which the host could suffer repeated attacks without developing immunity, but the work of Burnet in Australia has upset that conception. His work indicates that the herpes virus once it has gained entrance to the human body persists in certain tissues throughout the life of the host. After the primary attack, which generally occurs in infancy, it lies dormant but capable of becoming active again at any time when the resistance of the host is lowered either by intercurrent infection or by other adverse conditions. To the biologist herpes would be an example of an almost perfect host-parasite adaptation. Other examples of such persistent latent infections have been demonstrated in various laboratory animals and it is quite probable that they may exist in domestic animals.

Marked differences in resistance to infection by different breeds of the same species are a feature of some virus diseases, a notable example being rinderpest in cattle. The resistant breeds appear to have been developed as a result of long exposure to the virus. British breeds of cattle, for example, have little or no resistance and the mortality when they are infected is very high, generally in the nature of 80 per cent. to 90 per cent. The cattle of the plains of India are much more resistant and mortality may be as low as 25 per cent. to 30 per cent.

Many methods are used for artificial immunization against virus diseases including passive immunization by the use of hyperimmune serum; simultaneous inoculation with serum and virus; the use of virus which has been inactivated by the action of agents such as formalin, crystal violet, phenol, chloroform, or by exposure to ultra violet light, and the oldest method of all, namely, the use of virus modified by animal passage, the so-called zoological modification.

Heat-killed vaccines which are so commonly used in immunization against bacterial diseases have not proved of any value against virus diseases.

It is the use of virus modified by passage through an unusual host which I wish to discuss to-day.

Jenner's method of vaccination against smallpox is the classical example and Pasteur's rabies vaccine is also based on it. It, therefore, has the longest history of any of the methods of immunization. It is curious that in spite of this long history and its established success in smallpox and rabies, it is only within comparatively recent years that it has been utilized in other diseases. It is of interest to note that this method is used only in diseases caused by viruses. None of the vaccines in use for immunization against bacterial diseases is made by this method.

The basis of the method is the artificial adaptation of a virus to an unusual host, this being brought about by repeated passage from host to host. Examples in use to-day are the goat-adapted rinderpest virus, the mouse-adapted horse sickness virus, the egg-adapted Newcastle disease virus, the ferret-adapted distemper virus and the egg-adapted rinderpest virus. This process of artificial adaptation of a virus to a new host is full of interest and a closer examination of one of these "adapted viruses," namely, the goat-adapted rinderpest virus, may prove of interest.

It was Edwards at Muktesar who developed this method as a practical means of control of rinderpest. When he started work the method in general use for the immunization of cattle against this disease was the simultaneous inoculation of immune serum and virulent virus. The source of virus was blood from an infected ox. A serious drawback to the method was that the blood might, and often did, contain pathogenic protozoan organisms such as species of Babesia, in addition to the rinderpest virus. In such cases heavy losses were likely to occur in the inoculated cattle. To obviate this danger, Edwards conceived the idea of utilizing the goat instead of the ox as a virus producer. The protozoan blood parasites of the goat do not infect the ox so goat's blood would be a much safer

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source of virus. His choice of the goat was probably influenced to some extent by the knowledge that the goat was known to be susceptible to infection with rinderpest. Natural outbreaks of rinderpest in goats were of rare occurrence but had been recorded. When Edwards attempted to transmit rinderpest to the goat from cattle by inoculation of blood, he found it was difficult to do so with any certainty. In his first attempts the infection, when it succeeded at all, was so mild as to be almost inapparent, little more than a short rise of temperature. With repeated passages, it became possible to infect with certainty and to produce a disease of considerable severity in the goat. Having reached this stage, he used goat blood to replace ox blood as a source of virus for serum-simultaneous inoculations. Later, after the virus had been passaged through goats for many generations, it was found that the goat virus without a protecting dose of serum, could be injected safely into cattle of certain breeds which had a considerable degree of natural resistance to rinderpest. In such cattle, the goat-passaged virus produced a very mild attack of rinderpest, with little or no mortality, which was followed by a strong and lasting immunity. Edwards then advocated the use of goat-adapted virus, without a protective dose of serum, as a practical method of immunization of cattle of such Indian breeds as were known to have a considerable degree of natural resistance to the disease. He did not advocate its use in cattle of highly susceptible breeds as in such animals the reaction was very severe and terminated fatally in many cases.

The method soon became popular in India and to-day has largely replaced other methods except where cattle or buffaloes of the more susceptible breeds are concerned.

The Indian results attracted Daubney's attention in Kenya and he obtained a supply of Edwards' goat-adapted virus. When it was used on Kenya cattle, the reactions were so severe and the mortality so considerable that it could not be used without a controlling dose of serum. The explanation seems to be that Kenya cattle are more susceptible than the Indian cattle. Daubney therefore attempted to produce his own strain of modified virus. He started with strains of virus from natural outbreaks of rinderpest in Kenya cattle and succeeded in adapting several of these to the goat. One of his strains, now generally known as Kabete Goat Virus, proved after many generations of goat passage to be sufficiently attenuated for use on the Kenya native cattle but was still too virulent for use on highly susceptible cattle of European breeds. Even to-day after many hundred generations of passage in goats, I understand that the Kabete Goat Virus is still too virulent for European cattle. Following Daubney's work in Kenya his strain of goat virus was introduced into other African territories such as Tanganyika, Uganda and Nigeria. A very curious feature of the history of the development of this method of immunization is that in most cases when first introduced into a new territory, very severe reactions with considerable mortality followed its use. This was the case in Nigeria just as had been the case when Edwards' virus was introduced into Kenya. In Nigeria it was only after a considerable number of passages in Nigerian goats that the virus became sufficiently mild to be used with safety for immunization of Nigerian cattle. It was also found in Nigeria that a certain breed of native goat was quite unsuitable for maintaining the virus. In these goats the virus died out, while in another breed it could be maintained with success. To-day the method is in general use in most parts of India, Burma and Africa.

When a modified living virus is to be used as a means of immunization, there are two questions which merit careful consideration. First—can the disease spread by contact from the inoculated cattle to other cattle or to animals of other species? And, secondly—is it possible for the modified virus to undergo a reverse process, as it were, and to regain its former virulence? In the particular case of the goat-adapted rinderpest virus, the virulence has been attenuated for cattle by passing it through goats, but by so doing its virulence for the goat has been exalted. It would, therefore, appear likely that the widespread use of such a strain of virus in cattle would involve the risk of infection spreading to goats, unless precautions were taken to prevent healthy goats coming into contact with cattle reacting to inoculation with the virus.

The first point which has to be settled is—can the reacting cattle pass on infection to other cattle, to buffaloes, to goats or to species of game which are susceptible to rinderpest?

On the question of transmission by contact to other cattle, the great majority of observers appears to be satisfied that this does not occur in the field. Millions of cattle have been immunized by this virus in India and in Africa without any precautions being taken to segregrate the inoculated cattle while they are reacting. One is justified in assuming that, had infection by contact been a common occurrence, there would be many examples recorded in the literature. A study of the literature however, reveals comparatively few. The examples which I have been able to find are as follows:—Shahi in the Annual Report of the United Provinces Veterinary Department for 1933-34, says, "animals got the infection by ingestion of contaminated foodstuffs." The Madras Veterinary Department Report for 1938-39—"fresh foci of infection were set up by contact with reacting cattle." The Burma Report of 1938 reports the same occurrence in the case of buffaloes. Idnani (1944) says only one outbreak, a mild one, is on record where infection was due to the goat virus. The Bengal Report of 1938-39 says that there was evidence of spread of infection from reacting herds. Pfaff (1939) says that in buffaloes spread by contact has been seen. Olver (1938) says instances have occurred where foci of infection had been started by goat virus.

These reports are all based on field observations and have all been made in India or Burma; no such examples are to be found in the African reports.

Accounts of laboratory experiments to test infectivity by contact are not numerous in the literature. So far as I can ascertain, nothing has been published from Muktesar on the subject. Cornell and Oongwonsi (1941) made some experiments under controlled conditions. They conclude that animals infected with goat virus are definitely less infective than in the natural disease, but they warn against complacency. They were able to infect one buffalo by injecting it with the nasal washings from a reacting calf. Daubney reports experiments on a small number of cattle which he considers to prove that infection by contact does not occur. The conditions of his experiment, however, did not involve extremely close contact nor do the cattle which he used appear to have been of highly susceptible breeds.

Mitchell and le Roux (1946) also studied the matter and concluded that infection by contact does not occur frequently. That it might occur was shown by the fact that one out of two cattle which they had drenched with faeces from reacting cattle developed the disease, Waddington (1945) reports experiments which seem to prove that contact infection does not occur but one animal which he injected with nasal washings from a reacting animal did develop rinderpest.

A consideration of the available evidence, both from the field and laboratory, justifies the conclusion that infection by contact from cattle to cattle is not a common occurrence. Pfaff (1939) suggests that it may not be so rare in buffaloes as in cattle.

As regards infection from cattle to goats the literature which I have seen does not give any information.

On the question of infection by contact from goat to goat, Mahajan in the reports of the Hyderabad Veterinary Department, 1932-33 and 1933-34 records an instance of a goat contracting infection by contact.

The possible infection of wild animals by contact with reacting cattle is naturally difficult to prove or disprove. Thomas and Reid (1944) investigated an unusual outbreak of a mild type of rinderpest in various species of wild animals in Africa in which the source of infection could not be determined but in which the possibility of goat virus being responsible was not definitely excluded.

To sum up, the bulk of the evidence points to the rarity of infection by contact. If infection by contact does not occur, we must assume either that the adapted virus is not excreted from the bodies of the reacting cattle or that it has lost its power to penetrate into the body of a healthy susceptible animal with which it may come in contact.

It is difficult to believe that the virus is not discharged from the body of the reacting animal. It definitely multiplies in the body of the host and at a certain stage of the reaction is abundant in the circulating blood. In many cases the reaction is severe and the inoculated animal shows nasal and ocular discharge and even blood-stained diarrhoea. In fact, a severe reaction reproduces all the clinical features of virulent rinderpest with the exception that ulceration of the buccal mucous membrane seldom occurs. These discharges must, one would think, contain the virus and le Roux's, Waddington's and Cornell's experimental findings quoted above confirm that belief.

If we accept that the virus actually escapes from the body of a reacting animal, then we can explain the rarity with which contact infection occurs only on the basis that the virus has undergone some change which has rendered it very inefficient in attacking or penetrating power. Such a change might possibly occur in the course of many generations of "needle" passage. Looking upon the disease as an example of a host-parasite relationship, one could conceive that the goat-adapted virus transferred for many hundreds of generations from host to host by the agency of a hypodermic syringe and needle could ultimately become very inefficient in gaining entry into a new host. At least there would be no stimulus to the parasite to perfect its mechanism for penetration. It may be that this is occurring with the goat-adapted virus.

Personally I am not satisfied that the virus has lost its power of attack so completely that infection by contact is an impossibility.

Experience of the occurrence of rinderpest in Ceylon during a period of over 20 years is interesting in this connection.

Until the year 1930, Ceylon had a history of repeated outbreaks of rinderpest starting in Colombo, the port at which cattle from India were imported. In 1930 importation of cattle from India was prohibited and within a period of three years rinderpest was eradicated from the whole island. This state of complete freedom from rinderpest continued from 1933 until 1943. Throughout that period goats were regularly imported from India. They were landed at Colombo, quaran..ned and then released for slaughter. No outbreaks of rinderpest in the imported Indian goats were ever observed in the quarantine station. In 1936 Whitworth and Rocker in Malaya reported that they had observed a mild form of rinderpest in goats on arrival at Singapore from India.

As a result of this finding, although rinderpest had not been observed in imported goats at Colombo, we considered it advisable to prohibit the imported goats being taken out of Colombo. Regulations were passed compelling imported goats to be taken straight to the Colombo slaughterhouse from the quarantine station.

This state of affairs continued until Japan entered the war and it became necessary to increase rapidly the garrison of troops in Ceylon. The army authorities imported large numbers of goats from India for feeding these troops. The goats were not slaughtered in Colombo but issued alive to military units scattered at many points throughout the island. It was necessary to issue the goats alive so that they might be slaughtered in accordance with the religious rites of the various Indian units. All would have been well had the goats continued to be free from rinderpest as they had in past years. Unfortunately, that state of affairs did not obtain and for some reason rinderpest which had been unknown in these animals in the past was found to be present in a severe form in a very high proportion of the batches of goats imported. Before long, outbreaks of rinderpest occurred in Ceylon buffaloes and cattle kept in the vicinity of military camps. Here we have an example of a disease becoming common in a species of animal in which it had been very rare in past years. Why this should have happened is not known with certainty. The circumstantial evidence suggests that the use on a very large scale throughout India of goat-adapted virus as a means of immunizing cattle may have been responsible. The facts as far as I can ascertain them are that rinderpest in goats in India was a very uncommon disease prior to the use of goat-adapted virus on a large scale for the immunization of cattle, but became increasingly common thereafter and in 1942-43 and 1944 it certainly was present in a very high proportion of the batches of goats brought to Ceylon from India.

If that be the correct explanation it is an indication of possible danger inherent in artificial adaptation of a virus to a new host. The process of adaptation attenuates the virus in so far as the original host is concerned but exalts its virulence for the new host and possibly also for other hosts zoologically closely related to the new host.

The Interference Phenomenon

In the study of immunization by means of these zoologically modified viruses, examples of what has been called the "interference phenomenon" have been observed. This term has been used to describe the finding, first observed in virus infections of plants, that infection with one virus may protect against infection by a related virus. The protection is something quite different from the classical immunity which results from the production of antibodies. In the classical type of immunity the injection of an antigen excites the production of antibodies which can be demonstrated in the blood. A time interval, generally related to the incubation period of the disease, is required before the antibodies are produced. The interference phenomenon is not dependent upon the development of antibodies. Two viruses, one of low virulence and the other highly virulent, can be injected simultaneously with the result, in some cases, that the virulent virus does not cause disease. Many examples have been recorded in laboratory experiments. Pfaff (1939) recorded that cattle which had been inoculated with goat-adapted rinderpest virus could resist infection with fully virulent cattle virus injected as early as 24 to 48 hours after the goat virus. Green in America claims that injection of dogs with his ferret-adapted distemper virus protects them against simultaneous injection of fully virulent dog-distemper virus. He goes further and produces evidence to show that the ferret-adapted virus has a curative effect when injected into dogs during the early stages of clinical distemper.

Much speculation has been aroused as to the mechanism by which this phenomenon is produced. One explanation which has been advanced and which seems to meet the case reasonably well is based on the fact that a virus is a compulsory intracellular parasite. Before the virus particle can multiply it must enter or attach itself to a living cell. This process is envisaged as something on the lines of a chemical combination in which two atoms can combine by means of appropriate linkages. Once the links on a particular atom are occupied, no more atoms can combine with it. The virus according to this theory would have a link which would fit a corresponding link on a certain type of cell and related viruses would have the same type of link. Once the link on a particular cell had been occupied by a virus particle, no other virus particle having the same type of link could attack that cell. The situation would be something like a key in a lock. So long as the key is in the lock, no other key, no matter if it fits perfectly, can open that lock. Green explains his findings in the case of distemper on this basis. In his experiments he infected dogs with distemper by instilling virulent virus into the nasal chambers. After the usual incubation period, the dogs developed the early clinical symptoms of distemper. At this early stage of the disease, Green injected a large dose of his ferret-adapted virus by the intramuscular route and claims that this had a curative effect on the dogs. His explanation is that the infecting virulent virus has to spread slowly from cell to cell in the body of the dog and it is not until a large proportion of the susceptible cells have been invaded that serious symptoms, or death, will occur.

In the stage of early clinical symptoms, only a small proportion of the susceptible cells have been invaded. At that point a large dose of the modified virus is injected intramuscularly. This favours rapid absorption and dispersal of the modified virus through the body and so gives the modified virus the opportunity to enter those susceptible cells which have not yet been attacked by the virulent virus. These cells are then blocked against attack by the virulent virus and so the chances of recovery are improved. The chief use of Green's modified virus is, of course, as a prophylactic rather than as a curative. For this purpose it is claimed to have a great advantage over other methods of immunization in that, because of the interference phenomenon, protection is conferred very rapidly. There is no negative phase and the vaccine may be used on immediate contacts and on dogs already in the incubation stages of distemper.

Before leaving the ferret-adapted virus, it is of interest to note that the non-infectivity by contact which we have discussed in the case of rinderpest is said to be also a feature of the ferret-adapted distemper virus. In the case of foot-and-mouth disease virus too, when the virus is adapted to the guinea-pig, these animals can readily be infected by inoculation but the spreading power of the disease may be modified.

It would, therefore, appear that loss of attacking power occurs not uncommonly when a virus is passaged for a number of generations in an unusual host by artificial means.

Epidemiology

Passing now from immunity to epidemiology, I wish particularly to consider some of the features of the spread of Newcastle disease of fowls.

The history of the disease is short as compared with that of many other diseases. The first mention of it in the literature is by Kraneveld in the Dutch East Indies in 1926. In the same year Doyle studied an outbreak of disease at Newcastle in England and published his findings in 1927. Features of the disease to which Doyle drew attention were its extreme virulence as evidenced by the short duration of illness and the mortality which approximated 100 per cent., and its differentiation from the well-known fowl plague. He showed that the cause was a virus which was immunologically distinct from the virus of fowl plague, that the disease was readily transmitted by close contact, that the virus did not, under natural conditions, survive for long outside the body of the fowl and that in the few birds which recovered a solid immunity resulted. In his original paper, Doyle, discussing the possible source of infection, stated that no other outbreaks of this disease had ever occurred in England and that no new birds had been introduced into the flock. Pigs were kept on the poultry farm on which the disease occurred and had been fed on swill collected in Newcastle. In discussing the differential diagnosis, Doyle mentioned the similarity in symptoms which the disease showed to outbreaks of disease in fowls which had been described in America under the names of Infectious Bronchitis, Laryngotracheitis, Coryza, etc.

Within a short time of the outbreak at Newcastle, outbreaks occurred in many widely separated parts of the world, for example in 1926 in Korea, in 1927 in India and Ceylon, in 1928 in the Philippines, in 1930 in Australia. Since then outbreaks have occurred in many other places and during the war the disease became widespread in many parts of the continent of Europe, for example, in Italy, Hungary, parts of Germany, etc., and in Africa.

In all these outbreaks, the mortality caused by the disease was very high, generally close on 100 per cent. The disease has certain points of resemblance to fowl plague but a feature of the early outbreaks was that they occurred in countries, with the exception of England, which had no past history of fowl plague. Another

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striking feature is that in many cases the initial outbreaks occurred at large ports, for example, Newcastle, Batavia, Colombo, Manila, Melbourne and Mombasa, a fact which suggests that shipping played an important part in distributing the disease.

Many of the countries, for example, India, Ceylon and the Dutch East Indies, in which serious outbreaks have occurred, are countries in which the wild jungle fowl is native. The jungle fowl is, of course, the ancestor of all our domestic poultry. If the virus of Newcastle disease originated in the jungle fowl in bygone years, one would expect fowls in the countries where that bird is native to have developed some resistance to the disease. That, however, is not the case. In Ceylon the village breed of fowls which is not far removed from the jungle fowl, is just as susceptible to the infection as improved breeds from Europe. The same was the case in India, the Dutch East Indies and the Philippines. To my mind this high susceptibility of the native fowls of these countries indicates that the original host of the Newcastle virus is not the jungle fowl, but some other species of bird. A curious feature of many of the earlier reports of outbreaks in India, Ceylon and elsewhere was mention of heavy mortality in wild birds, particularly in crows, occurring simultaneously with outbreaks in fowls.

Up to the year 1944, although outbreaks had occurred in Europe, Asia, Africa, and Australia, in all cases characterized by extremely high mortality, no outbreaks had been reported from the American continent

Doyle, in his first description of the disease, had noted the similarity in symptoms which existed between Newcastle disease and certain respiratory infections which had been described in America under such names as Infectious Bronchitis and Laryngotracheitis. In the interval between 1927 and the present time, infectious diseases of poultry characterized either by respiratory or by nervous symptoms or by both have been described in America under various names. For example, nine-day pneumonia or chicken 'flu were said to have been present in Califonia as early as 1935. Stover in 1942 described a respiratory nervous disorder of chickens in Californa. Another disease called avain encephalomyelitis or epidemic tremor, had also been described. Pneumoencephalitis of chickens had been studied by Beach and others. These various diseases all bear points of resemblance to Newcastle disease but differ from it very strikingly in the much lower mortality. Instead of a mortality approximating 100 per cent. which had occurred with Newcastle disease in England, Asia, Australia, the continent of Europe and in Africa, the mortality was low. In 1944, Beach announced that he had proved that the virus which was the cause of pneumoencephalitis of chicks in California was immunologically identical with Newcastle disease. Stover's "respiratory nervous disorder of chicks" has also been proved to be the same as Newcastle disease. Laryngotracheitis has been shown to be due to a separate and distinct virus. Coryza of fowls has been proved to be caused by a bacterium, *Haemophilus gallinarum*. The question of the identity of the infectious bronchitis of chickens which Doyle had noted in 1927 as resembling Newcastle disease does not appear as yet to be quite satisfactorily settled. Stover in 1942 studied its relationship to what at that time he called "a respiratory nervous disorder" virus. He did not use large numbers of birds and reports that 19 chickens which had recovered from infectious bronchitis proved to be susceptible to the "respiratory nervous virus" but that 50 per cent. of chickens immune to the latter virus were refractory to infectious bronchitis. That evidence does not appear to be sufficient to separate the two viruses with certainty. Since then the "respiratory nervous virus" has proved to be Newcastle virus. Brandly, Moses, Jungherr & Jones (1946) in a paper dealing with the isolation and identification of the Newcastle virus in America, consider that the infectious bronchitis virus is separate and distinct from the Newcastle virus but the experiments on which they base their opinion are few in number and not altogether convincing. They challenged with Newcastle virus twelve pullets believed to be immune to infectious bronchitis—and all twelve died. These twelve pullets, however, were not satisfactorily proved to have been immune to infectious bronchitis. It is stated that "they were pullets from a flock which had been exposed on range shortly before placement in laying houses." It would seem to be necessary to repeat this work using birds which had been definitely infected with the infectious bronchitis virus before it can be assumed that the two diseases are actually separate and distinct.

Epidemiologically, the great interest of the American outbreaks of Newcastle disease lies in the different manner in which the disease behaves in that country as compared with other parts of the world. In Asia, the outbreaks were dramatic in their violence and attracted immediate attention as something new and unprecedented. The same was the case in England, Australia and Africa. On the continent of Europe the disease was at first confused with fowl plague, the only other known disease of poultry which approached it in violence. In America, on the other hand, its mildness resulted in its being unrecognized for years. One obvious conclusion which might be drawn from these facts is that fowls in America have had much longer contact with the virus than fowls in other parts of the world. As I have said earlier, the native breeds of fowls in Asia proved to be highly susceptible to the infection. Asia is the home of the jungle fowl, the ancestor of all our domestic breeds of fowl. So it would appear that the jungle fowl is not the original host of this virus.

The fowl is not indigenous to America. It was introduced into that continent by the early settlers from Europe and the fact that fowls in Europe have proved to be so highly susceptible to the virus appears to indicate that the virus was not introduced into America along with the early settlers' fowls. In that case, the probability is that the true or original host may be some wild non-migratory bird native to America. If that supposition should be correct then one would expect that what has happened is that the virus, originally a parasite of some American wild bird, has adapted itself to attack the fowls introduced into America some hundreds of years ago and at the same time the fowl in America has, to a considerable extent, developed a resistance to the virus, accounting for the low mortality in that country and the very high mortality when the virus is introduced into other countries.

This very brief survey of Newcastle disease illustrates several important epidemiological features, among them the high mortality which may occur when a new virus is introduced into a susceptible population, the rapidity with which infection can be spread over great distances by modern transport, and the fact that transport of living animals is not necessary for the spread of infection. In none of the initial outbreaks of Newcastle disease in England, Asia, Australia or Africa, was there any evidence that infection had been introduced by live poultry. That this should be possible is doubtless due to the fact that the virus in the carcases of table poultry is capable of survival for long periods at low temperatures.

The most probable way in which the rapid and world wide dispersal of this disease has occurred is by means of offal containing portions of fowl carcasses being landed from ships at large ports and used for swill feeding of pigs and poultry.

Summary

The conception of a virus disease as a manifestation of a host-parasite relationship is stressed. The use of zoologically modified strains of virus as immunizing agents is discussed with special reference to the goat-adapted rinderpest virus and the reduced infectivity by contact of such modified viruses is commented upon. The possible danger of extension of the host range of a virus by the indiscriminate use of artificially modified virus is pointed out. The interference phenomenon and its role in immunity to virus disease is briefly discussed and illustrated by reference to rinderpest and distemper.

The rapidity with which a virus disease may be disseminated throughout the world under modern conditions is illustrated by a description of the spread of Newcastle disease of poultry to all five continents since it was first recognized in 1926. The different behaviour of the disease in America as compared with other countries is described and the possibility that the true host of this virus may be some species of American wild bird is suggested.

Discussion

Dr. W. M. Henderson (Pirbright): I am glad to be the first to congratulate Mr. Crawford on his most interesting paper. I am fortunate enough to live in the same part of the country as he and he makes our frequent discussions invariably stimulating and interesting. His paper has repeated that standard, that high standard in fact, that we have come to expect of anything emanating from the Imperial Bureau of Animal Health.

Mr. Crawford begins by accepting the hypothesis that viruses are living entities and he sees fit to consider a virus disease from a general biological point of view rather than merely from a pathological aspect. I am in complete agreement with this method of approach. There seems to be no acceptable alternative to the concept of a virus as a living organism which, in common with all living things is possessed of that immense potentiality for survival, the necessity for perpetuation of its species. This demands inclusion of the study of the ecology of viruses in any consideration of the diseases they cause. It is only by such wide consideration of the infective agent that we can come to a fuller understanding of a disease. Neglect of this aspect to the more obvious claims of pathology will leave us unprepared for many disappointments and will tend to make many problems appear insoluble. This is by no means an original point of view, it has been much more ably expressed before, most notably by Charles Nicolle in "Destin des Maladies Infectieuses"[1] and more recently with particular reference to virus diseases by Burnet in his Dunham Lectures at Harvard

University in 1944, now published as a monograph "Virus as Organism."[2]

Mr. Crawford has quite rightly drawn attention to the varying duration of immunity to different virus diseases following natural infection. In studying this aspect experimentally it soon becomes apparent that the estimation of immunity can only be relative to the conditions of test. Following an efficient stimulus of the antibody producing mechanism by natural attack of the disease, immunity may appear solid and prolonged if the portal of reinfection is such that the virus is exposed to the circulating antibody before it can reach the sites of predilection for manifestation of the disease. Such is usually characteristic of a viscerotropic or a neurotropic virus infection transmitted by means of an insect or an arachnid. The virus introduced into the peripheral circulation is fully exposed to the action of the circulating antibody before it can reach the susceptible cells, but as louping ill is an example I have no doubt Dr. Wilson will have something to say on this point. If the virus can gain the susceptible cell without being exposed to circulating antibody then immunity may appear to be more transient as the virus can usually establish itself and possibly induce some signs of clinical infection. This can be demonstrated experimentally in foot-and-mouth disease in that a recovered animal is capable for many months of resisting infection by contact or by subcutaneous or intramuscular inoculation. If, however, the test of immunity is the direct introduction of the virus into the susceptible cells by an intra-epithelial injection of the tongue then the animal may be capable of resisting this only for a comparatively short period of weeks. A local lesion arises at the site of inoculation but no further development takes place, since before the infective agent can reach other sites of predilection—for example, the feet—it must enter the blood stream where the circulating antibody can deal with it and prevent further extension.

In certain virus diseases it sometimes proves impossible to demonstrate the presence of circulating antibody in animals that subsequently resist exposure to infection and this has led to a concept of "tissue" as distinct from "humoral" immunity. In this connection, however, it must be remembered that the possibility of demonstrating the presence of antibody is, in certain cases at least, determined by the sensitivity of the test employed and my colleague, Dr. Brooksby, by means of a specially sensitive method evolved by him for the detection of foot-and-mouth disease antibody, has recently demonstrated neutralizing antibody in the blood of cattle no less than two years after infection, a new fact of some importance in immunology.[3]

In considering the mechanism of the "Interference phenomenon" Mr. Crawford cites the thesis similar in most respects to Ehrlich's side-chain theory of immunity. We cannot do more than speculate about the possible mechanism of the interference phenomenon as we know nothing about the nature of the reaction between virus and susceptible cell. It is strongly suggestive, however, that under certain conditions, cells can be invaded without subsequent virus multiplication but with the development of a resistance to certain other virus particles. The development of this resistance might well be the utilization or the fixing of some cell component necessary for multiplication of the other virus; whether this material be a metabolite or of the nature of complement remains to be discovered.

The problem of the origin of the rinderpest infection in the goats reaching Ceylon is a very controversial one and I wonder if the greatly increased number of troops in India during the war brought about new and increased movements of stock such as Mr. Crawford has described for Ceylon, thus giving greater opportunity for the spread of endemic disease. In which case might not the increased incidence of the disease in goats be due, just as likely, to bovine virus as to goat virus? Although I have had the privilege of working for a number of years in the same Institute as Dr. J. T. Edwards, recently described by an enthusiastic journalist as "The Man who Raised the Curse of Moses," I do not feel competent to pursue this question further and in any case I doubt if we *can* go much further without the results of a detailed examination of the characters of the virus strains in question.

In connection with adaptation of virus to an unnatural host, Mr. Crawford mentions the guinea-pig and foot-and-mouth disease, saying that ". . . these animals can readily be infected by inoculation but the spreading power of the disease may be modified." This may lead you to believe that the disease spreads among guinea-pigs before a virus strain becomes modified by passage; this is not so, the guinea-pig is at all times completely resistant to transmission of the disease by contact. It is true, however, that the infectivity for cattle of some strains can be markedly reduced by long serial passage in the guinea-pig but this quality has not so far been fixed. A more promising line of research in this connection has been the reported establishment by German workers of strains of virus in the mouse brain accompanied by loss of dermatropic properties.[4] There is no indication so far of the possibility of using such apparently modified strains of virus for immunization of other species.

Mr. Crawford makes more than one reference to resistant breeds, resistant species and resistance as the result of long association with a virus. In suggesting that a particular breed of a species or the population of a particular region is, by long association with the infective agent, resistant to the infection, we must have a very clear picture of what is meant if we wish to avoid basing conclusions on more than one fallacy. It is convenient to consider three forms of resistance. Firstly, the type of resistance found in animals to measles of man, in other animals to swine fever and to vesicular exanthema of swine, in the horse to foot-and-mouth disease and so on where resistance is presumably due to some physico-chemical feature of the host cell making it an unsuitable environment for survival or multiplication of the virus. Secondly, there is the resistance temporarily the result of a recently infected population and, thirdly, there is the resistance of a particular breed following long association with the infective agent, a form for which it is more difficult to find examples, the best perhaps being the negro for yellow fever and the plains cattle of India for rinderpest. I do not intend to discuss the theories of evolution but I believe that in considering this third form of resistance there is a danger of inadvertently accepting the Lamarckian view of inheritance of acquired characters. I prefer to think that the resistant breed may be evolved in nature by "survival of the fittest" and that the resistance is inherited, but inherited possibly by some genetic factor that may be only accidentally associated with the resistance to infection.

In connection with Mr. Crawford's suggestion that long association with the virus explains the low mortality of Newcastle disease among American poultry, I should like to take the opposite view that the low mortality results from a character of the virus and not from a character of the host. What we regard as the classic picture of Newcastle disease in which there is high mortality is a host-parasite relationship very prejudicial to survival of the virus and perhaps the characters of the disease in the United States indicate the progress of a variant towards equilibrium between host and parasite, a disease with a low mortality or even inapparent infection giving much greater chance for survival of the infective agent. One would like to know the results of cross-infection tests between American and European virus strains and European and American fowls. Before leaving the subject of Newcastle disease I should like to draw attention to Burnet's work in which he found a similarity between Newcastle disease virus and his laboratory strain "M.E." of influenza virus and his conclusion that the influenza group of viruses and Newcastle disease virus are related.[5] This may be of some significance in considering the origin of Newcastle disease.

While on the question of host-parasite relationship and its influence on the chances of survival of the parasite I should like to trail my coat in front of Dr. Wilson by being so bold as to speculate about a disease to which he and his colleagues have devoted much attention, namely, scrapie of sheep. We are told that scrapie is caused by a virus and that the incubation period of the disease is exceptionally long. Might it not be that the sheep showing clinical signs of scrapie is the exception, the one in which the virus had invaded tissues not normally infected in contradistinction to an association of the virus and host with the virus living, perhaps, an almost saprophytic existence? A saprophyte, however, impossible at this stage of our knowledge to detect. One can support this view by referring to poliomyelitis and cerebrospinal meningitis of man in both of which it is now commonly regarded that the clinical cases of paralysis and meningitis are the exceptions in an otherwise almost saprophytic relationship between the virus and the host and the meningococcus and the host.

I should now like briefly to refer to some aspects of the immunology and epidemiology of virus diseases that have not so far been mentioned.

The first is that feature of many virus diseases of animals, the occurrence of more than one immunological type where immunity acquired to one type leaves the host fully susceptible to infection with strains of another type. As examples we have foot-and-mouth disease, at least three distinct types; vesicular stomatitis, two types; vesicular exanthema of swine, up to four types have been recorded; equine encephalomyelitis, at least three types; horse sickness, probably more than one type; canine distemper, a Dutch worker, Verlinde,[6] has recently claimed to have isolated a strain immunologically distinct from the classic strains. The occurrence of completely distinct types is, of course, of great importance in the epidemiology of the disease and also a great

handicap to the research worker attempting to devise practicable methods of artificial immunization.

We have found in our work at Pirbright that distinct differences exist between strains of foot-and-mouth disease virus as regards their antigenicity when inactivated, their ability to stimulate an immunological response varies between quite wide limits. For example, using various strains the dose of inactivated virus vaccine necessary to produce the same response, 50 per cent. protection, in groups of cattle is: strain 119, 8 c.c.; strain ASJ, 26 c.c.; strain 39, 50 c.c.; strain 476, 50 c.c.; and we have evidence that the dose necessary with some strains may be even greater.[7] It has been suggested that, with an infectious disease associated with strains of different immunological types, a practicable method of control would be to isolate the strain of virus from an initial outbreak and from it prepare vaccine for use in controlling spread of the disease from that outbreak without first determining its type and then using a stock type vaccine. The significance of the results I have quoted is that it demonstrates the necessity of studying the antigenicity of a strain and not assuming without trial that it will be suitable for preparation of vaccine.

Recently we have been working with a strain of foot-and-mouth disease virus isolated from the present series of outbreaks in Mexico and although by the routine methods of test this strain can be classified as Vallée A type, cross-immunity tests of different kinds have shown that it differs, in some measure, in antigenic structure from a stock Vallée A type strain. Its behaviour points to the possibility of having variation in antigenic structure between strains of the same immunological type. This may prove to be similar to the differences in antigenic structure found between strains of influenza virus of the same immunological type. This same Mexican strain has a number of other interesting characters one of which is its ability to produce an inapparent infection on quite a large scale; for example, of 33 susceptible cattle exposed to infection by contact with this strain 18 reacted with clinical foot-and-mouth disease whereas the remaining 15 showed no visible reaction but were subsequently found to have developed some degree of immunity approaching in many cases the degree of immunity resulting from natural infection.[8] It is unnecessary to stress the importance of considering these observations in a study of the epidemiology of the disease. One point of interest is to consider the behaviour of such a strain in connection with the waning of epidemics and the occurrence of sporadic outbreaks of the disease that fail to develop epidemic proportions. The decline in the number of outbreaks during the waning of an epidemic is often assumed to be due to the decrease in the number of susceptible animals following infection of the majority of the population; although this will undoubtedly be of importance we cannot discount the fact that the lability of the virus may be such that the character of the strain may change during the course of the epidemic and although still capable of spreading to susceptible cattle, may fail to produce more than some degree of immunity. In the same way the failure to spread of sporadic outbreaks of the disease in the intervals between major epidemics has been attributed to the presence of an immune population but one can see how a strain similar in character to this Mexican strain might produce the same picture in a susceptible population.

The preceding remarks will show that in my view an essential thing to remember in studying the immunology and epidemiology of virus diseases is that the infective agent is a living organism. As such it is subject to variation; it is capable of mutation with the evolution of entities by no means similar to those of preceding generations and this lability must always be considered in relationship to the ecology of the parasite and the host.

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Dr. D. R. Wilson (A.D.R.A., Moredun Institute), who was the second opener of the discussion, said: I would like, first of all, to express my thanks to Mr. Crawford for giving us this thesis, "The Immunology and Epidemiology of some Virus Diseases," and for presenting it in so interesting a manner. If I felt any disappointment after reading the thesis it was one rather of regret that, of the animal diseases mentioned, I had seen only distemper of dogs and of the others my only encounter had been with influenza, but in this instance it was purely a personal matter between myself as host and virus as parasite.

While I was thus at a disadvantage with regard to the diseases chosen for special consideration, that to me serves as a reminder of the vastness of the field of viruses and virus diseases, and while I beg to stray, in the main, from the confines of the subject of rinderpest and Newcastle disease, it is in the full belief that any virus disease or even a particular aspect of one is the concern of us all and therefore pertinent to the moment.

Many aspects relative to the subject matter of the paper have been very ably discussed by Dr. Henderson and need not be further commented on by me. However, with reference to the interference phenomenon I would like to ask Mr. Crawford what his views are in the case of viruses which are not related immunologically, for I understand that this phenomenon may occur by using the combination of yellow fever virus and Rift Valley fever virus injected intraperitoneally in mice.

In discussing immunity and the various methods that may be used for artificial immunization against virus diseases I can appreciate, as pointed out by the author in the case of rinderpest, the many advantages that accrue from the use of an adapted virus. Many people are keenly interested in this aspect for there is no reason not to believe that every virus is capable of mutational change. Perhaps one of the most notable is that which is being used for immunization of human beings against yellow fever. A pantropic or natural yellow fever virus strain was induced to grow in a particular medium and then in a second medium in which originally it had been unable to grow. In the first medium continued cultivation resulted in a marked diminution in the viscerotropic characters of the virus but the neurotropic properties were retained. In the second medium there was no further change but in a third medium which was a modification of the second further change took place but only after long cultivation. The virus had now lost, or at any rate there was a marked diminution in, the neurotropic properties. The strain of virus, originally virulent, had lost to a large extent both its viscerotropic and neurotropic characters and can now be used for immunizing human beings against yellow fever: simultaneous administration of immune serum is not necessary.

Some years ago I had the opportunity to carry out a few experiments with the virus of Russian spring-summer encephalitis. This virus, when first discovered, was thought to be identical to our louping-ill virus and in cross-neutralization tests carried out in America and later confirmed by myself it was obvious that in antigenic properties the two viruses possessed something very much in common. But Russian spring-summer virus was not obviously pathogenic for sheep on injection either by subcutaneous or by intracerebral route. When injected subcutaneously in large doses, although no temperature was produced and no other evidence of multiplication could be obtained, it had the effect of actively immunizing against a test dose of louping-ill virus. With respect to sheep this strain therefore could be regarded as an avirulent strain of louping-ill virus and as such could be used for immunizing sheep against louping-ill. If such were attempted with the Russian strain, however, what would be the implications? How soon afterwards would veterinarians or stockmasters accidentally prick themselves with syringe needles and subsequently contract a fatal encephalitis? How long would it take for our tick populations to become carriers and spread the infection in ever-widening incidence in mouse and vole populations or in human beings? I understand that approximately 30 per cent. of infections in the human subject prove fatal.

One naturally would doubt the wisdom of using a virus like Russian spring-summer encephalitis, louping-ill or equine encephalomyelitis in an attenuated form for active immunization of animals without first being very certain they had not acquired any enhancement of the virulence which they already have for man. The situation of course does not arise at present, for so far as I know there does not exist an attenuated form of any one of these viruses for its natural host.

It is curious that louping-ill virus should have retained its neurotropic properties in its natural habitat—sheep to tick and then sheep and so on alternately—when such a character is of no apparent benefit to itself and certainly none to its host. I cannot see that that fraction of virus which reaches the brain tissues and multiplies there plays any part in the survival of its species, for by the time it multiplies and escapes from the brain its host, if still surviving, will have developed a considerable titre of humoral antibody and this is quite capable of ending any further opportunity for survival.

Under experimental passage of virus—sheep brain to sheep brain—say for maintenance of a stock strain, where the sojourn in the tick is eliminated one might expect enhancement of the neurotropic properties with decreased ability to multiply in visceral tissues. In my experience, however, a stock strain of louping-ill virus maintained for 17 years has shown no observable change in pathogenic properties either for sheep or mice. The same strain cultivated in a chick tissue medium over a period of eight years without a single passage in a living animal has also remained unchanged. So far louping-ill virus strains, whether obtained from the north of Scotland or from Yorkshire, appear to be of the same immunological type.

I now wish to say a few words on neutralizing antibody which is present in immune animals and how it plays a very important role in the epidemiology of louping-ill. When a ewe possesses serum antibodies she is able to pass them to her lamb by way of the colostrum. They pass in great quantity and the lamb, although possessing none at birth, acquires, in a matter of a few hours after sucking, humoral immunity about equal in degree per c.c. of serum to that present in its mother. Such an acquired passive immunity in a lamb was found to be a very effective one and the administration of moderate doses of louping-ill virus by subcutaneous route had no apparent effect whatever. From these moderate doses of virus (about 40,000 M.I.D.) active immunity does not develop for the titre of antibody in the lamb's blood falls at the same rate as in similar immune lambs which had received no test dose of living virus. When lambs were about twelve weeks old humoral immunity had completely disappeared. A state of susceptibility to infection now existed as was shown by again administering a moderate dose of living virus. The first dose of living virus, as indicated, had had no effect whatever, for the lambs in this group reacted to their second dose of virus also given subcutaneously just as severely as did those which had not been subjected to the earlier test infection. The proportion of lambs receiving immunity from their mothers, is likely to vary on the different farms to some extent. It was astounding, however, to find that of the three- to five-year-old ewes examined, proportions of over 90 per cent. on each of seven typical louping-ill farms in the Border country possessed considerable titres of humoral antibody and they would, undoubtedly, have transmitted these antibodies to their lambs in the colostrum. In an actively immune animal humoral antibodies persist for a very long time, and a ewe which passes antibody to her lamb is capable of passing equally great amounts to her next lamb a year later without having had, in the interval, any antigenic stimuli from virus transmitted by ticks or experimentally by injection.

By virtue of the knowledge concerning maternal transmission of immunity, I do not think any purpose would be served by vaccinating young lambs, for those that are passively immune would be no more likely to develop active immunity from vaccination than similarly immune lambs had been from administration of living virus. Vaccination of young stock should be delayed until all trace of acquired passive immunity has disappeared and this is towards the middle or end of August. A second dose of vaccine can be administered with great advantage. Two doses are necessary before actively produced antibodies appear in the blood stream but I must admit the high antibody titres found in ewes are not wholly derived as a result of vaccination but arise from a subsequent mild attack of the disease or as a result of repeated antigenic stimuli from virus which is transmitted naturally by the ticks.

Scrapie.—I wish now to say a few words on scrapie, but I would like it to be understood that apart from passaging the infection in sheep the only experimental work I have carried out was designed to confirm or determine the filtrability of the infective agent. For this purpose three groups of sheep were injected intracerebrally with scrapie brain suspension and the dose administered to each sheep was 1 c.c. The respective groups received unfiltered suspension, filtrate from a gradocol membrane of 0·65μ A.P.D. and the third group a filtrate from a membrane of 0·41μ A.P.D. The groups were kept in separate fields which were not adjoining so as to prevent the animals in the different groups from coming in contact with one another. Briefly, the result was that scrapie developed in each group but the incidence of cases was not high. Four out of 18 animals which received the unfiltered suspension developed scrapie, this making an incidence of 22·2 per cent. In the other groups ten out of 36 animals receiving 0·65μ membrane filtrate developed scrapie, this being an incidence of 27·7 per cent., and seven out of 29 animals which received 0·41μ membrane filtrate developed scrapie, this being an incidence of 24·1 per cent. It was not possible to determine the size of the infective agent from this experiment because an end point in the filtration had not been determined. Filtration with the particular membranes used did not, however, reduce the infectivity of the suspension and it is possible that the virus is small in size.

A feature of the experiment was that most of the scrapie cases developed within a fairly well-defined period of time. One animal developed scrapie after an incubation period of five months while one case developed after an incubation period of approximately nine months. Most of the animals (21 in all) developed scrapie at about six months after injection—the average incubation period in the first group was 5·7 months, in each of the second and third groups 6·3 months. The duration of the disease was quite short and most of the affected animals died or had to be destroyed on account of paralysis after a course, averaging in the respective groups, eight weeks, six and a half weeks and seven and three-quarter weeks. Symptoms of intense itch predominated in all affected animals. Sixty-two of the 83 animals remained well up to the time when the experiment was discontinued; this was at one year after the injections were made because I felt that cases developing after that time (*i.e.*, twice the average incubation period) could readily have contracted the infection from contact with their affected neighbours. Whether these 62 animals suffered an inapparent attack of scrapie, *i.e.*, one in which there had been set up a harmony betwen the host and virus, is not known, for I was not able to destroy, say, half of them and carry out subinoculations in other groups of sheep nor had I any available biological test from which I could have determined whether they had acquired any immunity to scrapie as a result of exposure to the infection.

The failure to infect a majority of the animals used in the experiment may have been due to a low infectivity (*i.e.*, a low virus content) of the suspension. On this point I have no information for I did not determine whether there occurred any decreasing infectivity following progressive dilution of the original suspension.

I believe that in further research in scrapie an effort should be made to determine the distribution of the infective agent in the tissues of the affected animal and how animals become infected one from another; it is not known how the infective agent enters the body, where it multiplies, or how it reaches the brain.

At present the infective agent is being passaged in series from sheep to sheep in the hope that a more virulent strain can be acquired. The possession of such a strain would be of great value to those engaged in the study of scrapie.

General Discussion

Dr. A. Ginsberg (Edinburgh): On the subject of virus diseases he would like to have the opinion of experts. The meat inspector of this country condemned the carcases of beasts affected by foot-and-mouth disease; but most meat inspection laws of the Continent passed the carcases as fit for human consumption, except the parts that were affected. Those were also fit for human consumption after they had been dipped into boiling water.

There was a tendency before the war on the Continent to get rather more strict in this respect and to approach the British methods of eradication but recently he had found an article published in the *Polish Veterinary Record* by the meat expert, Professor Trawinski, who did some research in the All-Russian Institute for Meat Hygiene in Moscow. According to his paper, he carried out research on 35 cattle, and found that the meat was not infective five hours after slaughtering, and he thought that every carcase could be consumed except the bone marrow and spinal cord because there he found some virus. If that was so, no doubt we should have to think it over and to change, in times such as these, the present meat inspection regulations covering this country, because it would help Mr. Strachey to increase the meat ration. If that was not so, however, he would rather support the Member of Parliament who, in one of the discussions in Parliament, asked Mr. Strachey what steps he is taking to prevent the introduction of foot-and-mouth disease by imported meat from the Continent. He wondered if Mr. Crawford could give some information on that.

Professor Van Der Plank: Dr. Henderson had spoken about the congenital immunity of the host in connection with the virus. He was an animal breeder and the congenital side of this question interested him very much, and he would ask Dr. Henderson if he thought that the immunity required for the mother was congenital or not. During the war he had an experiment with white mice used for breeding the virus of typhoid, and it was found that they were not so good for the purpose as wild mice, and typhoid was not spread by the mice. He understood that it was a congenital question and not a question of survival of the fittest.

Dr. J. B. Brooksby (Pirbright): He had read Mr. Crawford's paper with very great interest and pleasure, and listened to the openers of the discussion with similar pleasure. He would like to reply to Dr. Ginsberg on the question of utilization of the meat of carcases slaughtered in foot-and-mouth disease. There was no doubt that the carcase of an animal slaughtered at the height of foot-and-mouth disease infection contained a large amount of

virus. This was contained in the infected tissues which had been attacked by the virus and also in the blood, so that all the organs were infected roughly in proportion to the amount of blood they contained, and therefore offal such as liver and kidney was highly infected, and would have to be destroyed.

He thought that the difficulty of avoiding contamination of material going off infected premises was almost insurmountable and the method referred to by Dr. Ginsberg was impracticable so far as this country was concerned.

There had been some remarks on the adaptation of virus to a species other than that which it normally affected. He would refer to some work which had been carried out at Pirbright on strains of foot-and-mouth disease which appeared to be adapted to one species.

This feature had been known for some time. There were several instances in the literature of strains of foot-and-mouth virus which infected swine and could either not, or only with great difficulty, be transferred to cattle. In this country in 1944, and since 1944, there had been a large number of outbreaks in swine. In some of these outbreaks the infection had been transferred to cattle. This transfer, however, had not taken place in very many of these outbreaks, so much so that it had even been suggested that the disease in swine was not foot-and-mouth disease, but perhaps one due to some other causative virus.

A number of these strains had been examined in guinea-pigs and it had been found that the virus from these outbreaks fell into one of the immunological types—in this case it happened to be "O." That was very good evidence for the strains being foot-and-mouth virus. In addition, in one case, the particle size of the virus had been determined and this also agreed with the strain being foot-and-mouth disease. In one case he had made experiments to transfer the infection to cattle and in agreement with the observations in the field he had found that it was not possible to infect cattle by contact with infected swine. On the other hand, it was possible to infect by inoculation of the virus into the susceptible tissues of the tongue. Once the virus had been established in a bovine it produced in many cases quite severe disease and he had had contact infection among cattle. The importance of this could be easily realized, for if by some mischance a porcine strain did get into cattle it was fully as serious as the cattle passaged virus.

Mr. G. C. Brander (Royal Veterinary College, Streatley): As there were quite a number of practitioners present he thought it might be worth while bringing up the vexed question of distemper. Most practitioners were finding that distemper serum virus immunization was not as successful as it was apparently five or six years ago, and he thought it might be interesting to find out if any of the speakers had any theories on immunity against distemper, whether it was effective or whether there was a second virus.

Speaking from experience during the war at the War Dog Training School, where there were at different times 700 or 800 dogs, it was the custom to immunize the dogs with virus serum. He thought perhaps it was done too soon after they were admitted, which was within 36 hours; but even so he did not think it should have led to so much trouble as actually arose.

It was found that in animals inoculated with virus serum, frequently within ten days almost 40 per cent. of them were liable to develop the symptoms one associates with distemper, that is, the various forms of catarrh, gastritis, and later the nervous forms. Despite the use of serum after the first development of symptoms, many dogs went on to develop an acute attack of the disease. He wondered if the speakers would suggest any cause for the apparent failure of the virus serum method of inoculation.

Brigadier J. J. Macfarlane Soutar (St. Andrews): Mr. Crawford's paper commenced with a statement which should be present in all their minds all the time when considering these problems, the fact that "all these virus conditions were essentially a manifestation of a host-parasite relationship and that such a relationship was not static but one capable of continual change." There were certain points in connection particularly with rinderpest on which he thought one might give some information which might be of value, not so much from the strictly laboratory or scientific point of view, but from the point of practical importance, in some of these diseases from which this country had been free for a very long time.

There was one statement with regard to goat virus in the paper which he thought might be corrected. That was that goat virus, when introduced, was not introduced primarily with a view to attenuation of the virus, but to filter the blood of the organisms which could be conveyed by using cattle virus. The other object was to enable the virulent material to be transferred over large distances and still be efficient in producing the reaction required. The goat virus could be sent in small quantities from the laboratory, inoculated on the site of inoculation probably thousands of miles away and the quantities required taken from goats on the spot and used for inoculation. Another point was that for a long time in the use of the goat virus in India serum had been dispensed with. Mr. Crawford said that Dr. Edwards recommended this method. His own recollection was that considerably after Dr. Edwards had left Muktesar, after doing some of the most valuable work that was ever done in connection with this disease, they continued using serum in inoculations and—this was a point of considerable interest—it was discovered that although in many cases there was very little reaction as a result of the serum simultaneous inoculation, yet even if there was no reaction giving visible symptoms, an immunity did develop.

He did not think that in a very long experience of rinderpest in Africa and in India, both before and after the use of goat virus, one could say that there was any great evidence to show that there was exaltation of the virulence of the virus to goats as a result of goat virus inoculation, and in that he disagreed with the suggestion in the paper.

Another point which he thought might be referred to was the very curious behaviour, in so far as immunity was concerned, of all methods of producing immunity in rinderpest. One could not produce immunity in a young animal, at least only for a short period, and it had afterwards to be reinforced. He did not know if that was paralleled in other virus diseases.

He would like to refer to and enlarge upon slightly Mr. Crawford's observations in connection with goats imported to Malaya and Ceylon. The imports before the war were on comparatively a small scale; they took place under well-controlled conditions, and any disease that occurred was dealt with straight away by destruction and nothing very much happened.

In 1941 Malaya had to be garrisoned with Indian troops and the local authorities ran up against the difficulty that goats, which seemed to be essential to preserve the military fighting virtues of some Indians, had to be imported from somewhere, and the only source from which goats could be imported in numbers was India. Steps were taken to get as many goats as possible from India. They were imported under conditions of extreme urgency, they were brought hundreds of miles to the port of embarkation with comparatively short periods of rest, the conditions on board the ship were appalling and there were great losses throughout the voyage. Rinderpest was not entirely responsible, other diseases were also present, but these goats conveyed rinderpest to Malaya, and the condition with which the veterinary authorities was faced was very serious. The problem was acute; it was foreseen that there was likely to be trouble when Japan did come into the war (and it was obvious that she was going to do so) and in order to increase meat resources of Malaya a very large number of cattle had been imported from the island of Bali, a little further to the east. Bali had had no experience, as far as was known, of rinderpest for over 100 years, which meant that a large number of highly susceptible cattle were being imported and the authorities were very much upset over the question of the goats bringing rinderpest into the country. The situation therefore was that they did not want any more goats to come in, but the Army had to have them, so something had to be done about it. The only solution which could meet both sides was to import the goats under conditions which made it possible for a considerable number to arrive alive and when they had arrived to treat them in such a way that they could not pass on the disease to the susceptible cattle.

Various things were started, including research into the method of immunizing these goats by a killed-virus method before the voyage started, supplementing that with a dose of serum in an endeavour to give a temporary immunity and to keep down infection during transit. Special quarantine stations were constructed where they could be given the attention they required, and afterwards they were transported to the troops requiring them, again under conditions which did not allow them to come into contact with local stock and to see that the troops dealt with them in such a way that they did not affect the local stock.

Things were doing very well when unfortunately the Japanese invaded and the matter ceased to be of practical importance.

Much the same things happened in Ceylon, but on a very much smaller scale, and he thought he was right in saying that the methods that were put into operation were successful in preventing a very large infection of the local stock in spite of rinderpest in the goats.

Dr. W. P. Blount (London): During and after the war, the table poultry industry in this country was comparatively small but it was supplemented by imported stock.

In the past two months the Ministry of Food had stopped the importation of Hungarian and European dead poultry, which meant that some thousands of shopkeepers were losing a very valuable

source of income and that the housewife had no alternative in that the few table poultry that came into the country passed into the "black market." The measure was taken, presumably, to prevent an occurrence of Newcastle disease, but the problem would be a simple one if the Ministries of Agriculture and Food prevented this by the use of an excellent vaccine which had been produced in India. He hesitated to stress who produced it, because, from the recent correspondence in *The Veterinary Record*, it would be realized Mr. Haddow, Sir Frank Ware and others had been concerned. If the vaccine were used in this country, it had been stressed it would be unwise because it would retain the infection, but he was assured that the reaction of the bird to the vaccine was a "silent" one and that there was not any question of vaccinated birds acting as carriers.

The second problem which arose was that the American form of the disease was immunologically different. Would this vaccine be of benefit against that disease because, although at the moment we were limited by dollars in the importation of American poultry, it might not be very long before we were running the risk of accepting American poultry with their low-grade type of fowl pest.

The present suggestion of the Ministry of Food was that carcases should be accepted minus head and feathers, but including the necks, and one assumed that a number of necks would pass into the swill pot and possibly avoid being boiled. He would ask the speakers if they could offer any suggestion as to whether the well-known "pullet" disease might from its epidemiology be considered to be of virus origin.

Mr. H. E. Harbour (Berkhampsted): He apologized for taking the discussion to the rarified air of the Scottish hill farm. On the hill farms both in Scotland and the North of England, there were three important diseases of sheep ; one was a virus disease, another tick-borne, and the third, which was probably associated with tick bite, tick pyaemia. What was going to be the effect of the impact of the new insecticides in tick control on the general immunity of the sheep on these hill farms to these diseases and to other diseases, including louping-ill ?

In the past it had been possible using the older type of preparation, arsenic particularly, to dip tegs at regular short intervals and to cut down the tick population by about 95 per cent. It had never been possible to do that with the pregnant ewe or the ewe suckling her lamb. Now there was a new era in which the new insecticides could be relied upon to give a much more prolonged protection. It was becoming possible to cut down very drastically the tick population of a hill pasture. Would this affect the host-parasite relationship—for he understood that perhaps 5 per cent. of the ticks might carry the louping-ill virus. What was going to be the effect of removing more than 90, perhaps 95 per cent. of the ticks ? Would the sheep become completely susceptible to these diseases and if subsequently a race of DDT-resistant ticks was developed, or ticks resistant to the new insecticides, would there be a very high mortality from louping-ill and other associated diseases ?

Tick-borne fever was closely associated with the incidence of louping-ill and in this case it was presumed that all the ticks which infested sheep could be expected to transmit tick-borne fever.

What would be the effect on the Scottish sheep of the drastic reduction of the tick population ?

Mr. J. E. Wilson (Lasswade) made no apology for re-introducing the subject of poultry. Some questions had been asked about immunity with regard to viruses and members might be interested in their experience in Edinburgh.

Dr. Greenwood at the Institute of Animal Genetics there had developed a line of Brown Leghorn fowls which were resistant to Rous sarcoma and it had been shown that this resistance was inherited. When injected with virus no growth of tumour resulted or if a small growth did arise it was followed by regression within a few days. This discovery was made by accident as in consignments of Brown Leghorn chicks used for cancer research, tumours regularly failed to develop in a number following injection with Rous material. Going carefully through his records Dr. Greenwood discovered that all these birds were from a strain which had been selected for "non-moulting." Thus birds possessing this characteristic were also resistant to Rous virus. As Dr. Greenwood's original stock consisted of four hens and a male from which by selection over many years he had produced lines giving small eggs, large eggs, small body size, large body size, non-moulting, etc., there was no question of the resistance arising from previous exposure to infection ; it appeared to be an inherited characteristic.

With regard to fowl paralysis, workers in this country and in America had produced by selection strains of fowls resistant and susceptible to the disease and it had been shown that these qualities were inherited. An outbreak was, therefore, probably determined by the degree of infection to which a flock was exposed in conjunction with its genetic constitution with reference to inherited resistance.

Dr. P. L. LeRoux (Dorking): One of the speakers had mentioned a natural resistance to infection, and he would like to ask Mr. Crawford to give some information or explanation of the resistance which Brigadier Soutar had mentioned in the case of young animals and rinderpest in India. In Africa this phenomenon was also manifested by both African and exotic breeds of cattle and their crosses and one could not immunize the young stock satisfactorily until they were older. Rinderpest was not the only disease in which that occurred, it had been observed in horse-sickness. The newly born foal was immune and could not be immunized until it had lost some of that "natural immunity." In the old days they were taught that the foal was immune or resistant if it had been born in the endemic area, because it had acquired antibodies from the dam's milk. More recent work had shown that it did not matter whether the foal was out of an immunized dam in the endemic area or out of a dam in a disease-free area. It was immune at birth and for some months after. In heartwater, a bovine disease transmitted by a tick and until comparatively recently regarded as due to a virus, the calf was immune whether it was born in an endemic area or not, but at the age of two to three months it began to lose that "natural" immunity and now was the time to practise immunization with success.

He would like to know whether there were any other diseases in which young animals exhibited a resistance and if a satisfactory and lasting immunity could be established in a susceptible animal without the provocation of a perceptible reaction to administration of the immunizing vaccine. He was associated with some of the rinderpest experimental work in the 1939-1943 "push" against rinderpest in Central Africa and in work to which Mr. Crawford referred, which he carried out in co-operation with the late Mr. D. T. Mitchell. It was found that it was possible to get an immunity without a perceptible reaction but that the immunity did not last quite as long as one would have liked.

Shortly afterwards he worked with contagious bovine pleuropneumonia, which was another malady which at one time was classified as a virus disease. Here it was noticed that if no reaction to the injection of attenuated virus resulted it might take as long as four months before an immunity was established and that that immunity lasted for only four months. In cases in which the batch of vaccine did cause a good reaction in all animals a solid immunity was established within three weeks and lasted for at least year.

He could not agree with Dr. Henderson—although he had probably had more experience than himself and had seen more of the literature—when he referred to the matter of tissue immunity in foot-and-mouth disease. He had at times in the past had to immunize (provoke the disease in a mild form) large numbers of cattle. It was a case of being forced into things which one did not like, but something had to be done to get rid of the disease. On one occasion 70 head of pure bred cattle (Sussex, Ayrshire and South Devon) had to be inoculated. The local native cattle and the grade stock had all reacted rather severely to the vaccine but he had read somewhere that when cotton wool was wrapped round the pads of the guinea-pig to reduce pressure on the pads this animal could be inoculated with foot-and-mouth disease virus without vesicles forming on the pads. He stabled the animals, bedded them down well and inoculated the virus intramucosally in the tongue. Not a single one of the 70 head developed vesicles on the feet although the reaction at the site of inoculation was marked and extensive. The story about the guinea-pig was true and the absence of the vesicles on the feet of the cattle must be attributed to the "soft" standing and not to any previously established local tissue immunity.

Parasites and viruses definitely manifested a predilection for certain tissues and certain organs. This was evident in the case of the vectors of mastitis. In cases of poll-evil and fistulous withers in horses and in cases of hygromas and enlarged tendon sheaths and bursae in cattle, the organism of bovine contagious abortion seemed to be attracted by the action of the nematode *Onchocerca cervicalis* in horses and *O. gutturosa* in cattle.

One of the first speakers had referred to the immunization of young lambs by vaccination of the pregnant ewes. This speaker contradicted himself in some of his statements. Some workers had reported great success by this method while others were much less successful. The data about the establishment of immunity or resistance to disease in the newly born by subjecting the pregnant dams to vaccination were unconvincing. He did believe that some good might result when the pregnant dam was susceptible to the disease, which might not be the case in an endemic area.

Working with various bacterial, virus and haemo-protozoal diesases of stock in Africa he had found that the greatest draw-

backs were that one was usually working in the endemic area. One never knew when one was dealing with truly susceptible animals. When he was working with contagious bovine pleuropneumonia in 1933-44 he insisted on having experimental animals from a known disease-free area and things came to light which some had branded as revolutionary. He set up the disease readily by pushing a thin needle through the chest wall and injecting the virus intrapulmonarily. Susceptible animals, kept in close contact with the experimentally infected cases, contracted the disease more readily than other workers had reported in the past. Being able to infect animals at will and thus knowing the exact age of the resulting sequestra, he was able to test the infectivity of the encapsulated material and had to conclude that all the statements about the virus remaining viable in the sequestra for months and months were merely fairy tales.

He welcomed Dr. van der Plank's suggestion that the question of breeding stock for resistance to disease by selection was worthy of attention. The development of resistance to disease was undoubtedly a physiological process which took place more readily in some animals than in others. It seemed possible that different physiological "build ups" of East African and West African cattle—two distinct breeds or races—might account for the differences exhibited towards attenuated viruses of rinderpest and contagious bovine pleuropneumonia. He thought that in some parts of the world improvement of stock would be best achieved by the selection of breeding stock for their resistance to disease rather than for abnormal high productivity.

Mr. D. D. Ogilvie (Manchester): He used to be an employee of the Ministry of Agriculture, but some years ago he managed to arrange his own liberation (laughter). While in the Ministry, contrary to general opinion, he learned quite a number of things, among them a very healthy respect indeed for foot-and-mouth disease. A few weeks ago he was on the Continent and was invited to go to an Institute where they were preparing the Waldmann foot-and-mouth disease vaccine. The initial part of the operation was being done in a small byre and when an accumulation of dogs and fowls had been driven out, he was shown a number of cattle which were salivating enthusiastically. Attired in the suit he was now wearing and without any protective clothing he was asked if he would like to examine the lesions in these animals. He was glad to say that with his Ministry upbringing he regarded this almost as an immoral suggestion and true to Ministerial tradition declined to take any action (laughter). He was due to return to this country next day but with the true interests of agriculture at heart he thought that this might be dangerous and accordingly managed to dally in Paris for a couple of days on the way back in order to let the virus die off (laughter). Quite seriously, he would like to ask the speaker and particularly Dr. Henderson, whether or not he considered that there was some danger of direct transference of foot-and-mouth disease from the Continent to this country by ordinary physical means. It should be remembered that one could now fly from London to several European capitals in little over an hour and even from Paris to Manchester in little more than two hours. He had questioned veterinarians in the country concerned as to the risks of spread of infection among their own animal populations but their answer had been merely that they found the Waldmann vaccine so effective and so many of their animals were now immunized with it that they had no fears in that direction. That did not apply, of course, to Britain. Incidentally, he would like to hear the speaker's views on the efficacy of the Waldmann vaccine, the use of which now appeared to be firmly established overseas. He would also like to learn whether any further progress had been made with crystal violet foot-and-mouth disease vaccine, about which little had been heard recently. Chemotherapy of virus diseases was, of course, still in its very early infancy and in this direction he would very much like to know whether any material advances had been made recently. The sulphonamide drugs, with early demonstrations of effectiveness against trachoma and lymphogranuloma inguinale, gave rise to hopes that compounds would soon be discovered which were active against a wide range of virus diseases but unfortunately those hopes, so far, had proved unfounded.

The Replies

Mr. Crawford, in reply to the discussion, said that when he was asked to write the paper the title suggested was "Recent Advances in Virus Diseases." He did not like that title for several reasons: one, a very good one, that he was not competent to handle it, and it would have involved very great labour; secondly, such a paper, in his opinion, tended to develop into a catalogue, which was very valuable for reference, but not so likely to promote an interesting discussion at a conference such as that. He therefore suggested that he might be allowed to deal with one or two of the virus diseases of which he had had some personal experience. The difficulty was that the one or two diseases with which he had had contact were not those which would appeal to people working in this country; but, knowing who was going to open the discussion, he knew that the field would be greatly extended, and this had proved to be the case.

Dr. Henderson had suggested alternative explanations for one or two of the things he had said in his paper. With regard to rinderpest in goats, Dr. Henderson suggested that it was unnecessary to postulate any spread of infection from the goat-adapted virus and a better explanation might be found in the conditions which occurred in India as a result of the war. This was a very reasonable suggestion, but against it he would like to put the point that in the previous war there were large troop concentrations in Mesopotamia and in India. The provisioning of these troops was done from India and large numbers of cattle and goats were supplied, but no rinderpest occurred in goats; at that time of course they did not use the goat virus. It could not be proved that the rinderpest in the goats imported into Ceylon was due to the goat-adapted virus. He was not suggesting that the goats arriving in Ceylon were actually infected with the goat-adapted strain. They were not. Had that been so the disease which resulted in the Ceylon cattle would have been much milder than it was.

Malaya and Ceylon for many years, as far back as the British occupation, had been importing goats from India in large numbers. Brigadier Soutar suggested that it was on a small scale, but scales were relative and the R.A.V.C. in the last war was apt to think in millions rather than in thousands. The scale was considerable from Ceylon's point of view. Prior to the war they were importing 100,000 goats a year into Colombo; during the war it went down as far as civilian goats were concerned, but when the military came into the picture it went up by thousands.

In Malaya the first hint that goats from India could be dangerous came when Rocker & Whitworth described an outbreak there in 1936. In that outbreak the rinderpest was mild and it was difficult to kill cattle with virus taken from those goats; the type of virus which was present resembled the goat-adapted virus. The 1941 outbreaks were different, the rinderpest in the cattle was virulent, so that it was possible that the goat-rinderpest virus had got into the goat and by passing from goat to goat by contact had regained, to a certain extent, its attacking power. Dr. Henderson suggested that the goat virus which was present was actually bovine virus, but the fact that it spread so rapidly in goats suggested that it was not.

So far as the African Colonies were concerned, one could not find an example in the annual reports of the Veterinary Departments of rinderpest in goats. There was plenty of rinderpest in cattle, they had plenty of goats in close contact with the cattle, but there was no record of rinderpest in goats, so that in Africa the natural bovine virus did not seem to attack goats.

He thought this was the proper stage at which to deal with Dr. Blount's remarks about Newcastle disease. Dr. Blount suggested that the Newcastle vaccine should be brought into use in this country. He (the speaker) thought that would be a very unwise thing to do. Dr. Blount was arguing, he thought, from experience in India. He said India had done it, why should we not do it, but conditions in India were not the same as in this country. Here we had a reasonable prospect of totally eliminating the disease by slaughter and police measures. Such measures were out of the question in India: they could not even be thought of. It was necessary therefore to fall back on to a second best method and use the vaccine. Dr. Henderson had told him that he understood that the vaccine was put into use in the field in India with very great misgivings on account of the fear that change in the virus might occur and virulence be regained, but it was the only measure available to cope with the situation. These were very different conditions from anything we had in this country, and he would strongly support the official view that vaccine should not be used.

Coming to the Newcastle virus, he had made the suggestion that possibly this virus might have originated in America, and that the different character of the disease in that country as compared with other parts of the world, might be deemed due to greater resistance on the part of the American fowl. Dr. Henderson took the opposite view and said that a better explanation might be that the difference was due to a difference in the virus rather than in the host. There, both of them tended to fall into error. They tended to forget that disease was the manifestation of relation between those two factors and that each reacted on the other, and the two should not be separated into watertight compartments. The interesting point as regards American experience was that in all other countries in which Newcastle disease had occurred it had been very virulent with a very high mortality, whereas in America it had been mild. Dr. Henderson suggested that America

was infected by a mild virus but, so far, no other country had reported such a variant virus. If it was a mild virus it must either have arisen in America or have been introduced into America. If it was introduced into America where did it come from? Was it introduced in the weaker state or the virulent state? If it was the normal state, the outbreak would have shaken America and there would have been a history of the spreading of the disease from a certain focus, but there was no such history. The disease was present and known under different names for some years before it was identified and centres of infection were found throughout the country. There was no picture of introduction and spread, so that there did appear to be a case for suggesting that it might have arisen in America.

The obvious need to-day was to test an American strain on the English fowls, and the English strain on the American fowls. That had been done to some extent, in the sense that English, Asiatic and European strains had been sent to America and studied, but he had not seen in the literature any clear or definite comparison of the mortality which these strains caused in the American fowls. A great deal of work had been done in America, but one did not get all the information about its behaviour in adult fowls that one would like to have, because much of the work had been done on chick embryos. Some of the American strains had been sent to this country, but unfortunately, Mr. Asplin, who had worked with them, was not present. So far as Mr. Asplin's work had gone, he understood that the disease produced in English fowls by the American strains of virus had been definitely mild, but the strains which came from America were all strains which had been maintained in the chick embryo for some generations, so that it was not possible to say anything very definite at this stage.

Dr. Henderson, speaking of the interference phenomenon, had suggested that the correct explanation might be that it was a question of one virus using up a constituent of the cell necessary for the multiplication of both viruses. In some recent work in America where workers were studying *Plasmodium gallinaceum* infection of the fowl, they found that if the parasite was injected into fowls fed on a diet which was deficient in pantothenic acid they could not be infected. That was very interesting and an example of a deficiency protecting the host against the parasite. That fitted in with Dr. Henderson's suggestion that interference might be due to competition between the two viruses for a constituent which was vital for their development. He thought that might be the answer to Dr. Wilson's question, when he asked if an explanation could be given as to why two unrelated viruses showed interference. The instance he referred to was interference between yellow fever virus and Rift Valley fever virus. All previous examples of interference which had been recorded concerned related virus, excepting the one which Dr. Wilson mentioned. There were two explanations which could be offered, one about which he had just spoken, namely, that these two viruses, although unrelated, might have similar nutritional requirements, and the other that quite possibly they were in fact related.

Dr. Wilson's remarks about the louping-ill virus were interesting. He had no experience of the disease, but what interested him was Dr. Wilson's remark that in 17 years of passage in sheep or mice, there was no evidence of any change in the virus. This was in marked contrast to many other viruses.

Dr. Wilson also brought up the question of immunity in young animals and the passage of antibodies from the mother to the young in the colostrum. It was known in many diseases other than the ones he mentioned and the point which struck him in listening to Dr. Wilson's remarks was that in louping-ill the antibodies passed to the young through the colostrum were present for as long as twelve weeks. This was strange if it was compared with antibodies passively transferred from one animal to another by injection of an immune serum. So far as he knew, with any serum so injected into a healthy animal, the antibody titre very quickly dropped and within ten days was down to a level where it was practically non-existent. In Dr. Wilson's cases antibody persisted for twelve weeks, which would indicate some difference between antibody in the colostrum and that in serum.

Dr. Ginsberg had spoken about foot-and-mouth disease and meat inspection regulations. The method of dealing with carcases infected with this disease was governed not by considerations of the infectivity of such meat for the consumer but from the point of view of spread of infection to livestock. The conditions under which foot-and-mouth disease-infected cattle and contacts were slaughtered rendered it very difficult, or impossible, to deal with them in such a way as to obviate risk of spread of infection if they were utilized for human food. Dr. Van der Plank had asked some question about genetics and resistance to virus diseases; all that could be said was that there was a lot of evidence accumulating which showed that it was possible in small animals to breed disease-resistant strains or disease-susceptible strains. As to how inherited resistance was developed he was not so unorthodox as to believe that acquired characters were inherited. He thought that Dr. Wilson's explanation was the more correct one, that the disease eliminated the susceptible animals and over a number of years one got a build-up of resistant types in the population.

Mr. Brander talked about distemper and the failure of the serum virus method in immunization during the war. This was a disease with which he had had little to do, but it resembled rinderpest very closely in many respects and if Mr. Brander's experience with the dogs had occurred with cattle and rinderpest, that is, within a short period after inoculation with serum and virus, the cattle had developed rinderpest, the first thing that one would think was that either the serum was of low potency or that the dose was inadequate to control the virus.

Brigadier Soutar corrected him on the point that the virulence of rinderpest for goats had been exalted by passage. He did not want to retract that. There was little doubt from Edwards' work that he found it difficult to infect the goats; it was only after a number of passages that he was able to set up severe disease and to infect with certainty.

Mr. LeRoux asked about the difficulty of immunizing young animals. The first point was the transfer of immunity from the dam through the colostrum to the young animal and its duration. If the young animal had a high antibody content, it would be difficult to immunize; on the other hand, the explanation might be found in the nutritional requirements of the virus. The young animal's metabolism was different from that of the adult, and it might be that an essential requirement for the virus was deficient in the young animal with the result that it was not until it was older that it became susceptible to the disease.

Mr. Ogilvie's remarks were interesting and showed what a high sense of duty the Ministry inculcated into its officers. Although Mr. Ogilvie was no longer an officer of the Ministry the training he had received still influenced him so that rather than run any risks of conveying infection he had put himself to the very great inconvenience of staying two days in Paris. (Laughter.)

In conclusion, Mr. Crawford wished to thank the speakers and especially the openers of the discussion for the very kind way in which they had dealt with his paper.

Dr. Henderson, also in reply, said that Dr. Van der Plank's question had been answered during the discussion, as Dr. Wilson's account of Dr. Greenwood's resistant strain of fowl illustrated the point he wanted to make. Might not this occur in nature? Under natural conditions the very susceptible would have been weeded out over a large number of generations.

With regard to Mr. Ogilvie's question on the efficacy of Waldmann's vaccine, this type of aluminium hydroxide absorbed vaccine had been used extensively on the Continent and it did have considerable effect in modifying the spread of the disease. But, in spite of the work done at Pirbright studying immunization methods, they were not prepared to say which was the best vaccine. It would be very foolish to attempt to answer that question. Foot-and-mouth disease vaccination must be considered according to the circumstances in which it had to be applied. The situation in each country was entirely different and many factors had to be taken into account.

Dr. Wilson, also in reply, said that he appreciated the question from Mr. Harbour and his first reaction was that the policy he would adopt in the event of a fall in the tick population would be to increase the number of doses of vaccine administered to the sheep to replace the antigenic stimuli which would be missing on account of falling numbers in the tick population. If it was possible to reduce ticks by 90 per cent (?) one would hope that perhaps Mr. Harbour would finally succeed in eradicating ticks altogether and in that case one would expect great reduction in diseases that were associated with tick bites.

Mr. Crawford asked the question as to whether he had expected there would be any change in the character or transmissibility of virus after a number of years. He asked whether the virus might not have changed with regard to transmissibility by the tick but he was sorry he had no information on that point. The virus had been maintained in the laboratory for 17 years but so far as he knew no very recent experiments with ticks had been set up to determine whether any change in the transmissibility of virus had occurred.

Passive immunity transferred from the mother to the lamb had also been mentioned. He had taken a great interest in this question. In experiments it was found that it could extend over a period of approximately twelve weeks and he thought that the long duration was a feature of passive immunity which was maternally transmitted. It had been found in other virus diseases that the duration was much longer than where a serum had been injected subcutaneously. Duration was in some way proportionate

to the amount of antibody initially present but not directly proportional. Antiserum injected into a lamb in a dose of 5 to 10 c.c. would result in immunity lasting only three or four weeks. If the amount of antibody was increased much beyond this the duration of immunity might last a little longer but it would not last so long as the passive immunity maternally transmitted. He knew of no real explanation of the phenomenon. It might be in part due to the fact that antibody, maternally transmitted, was as homologous as one could ever expect it to be.

He thought Dr. Le Roux also asked a question *re* passive immunity. He could not quite catch the point he was making but understood it to be that an animal that had passive immunity could not be immunized. In experiments in louping-ill at Moredun, animals possessing a very efficient degree or high-grade passive immunity did not develop active immunity from administration of an amount of virus which was within reason. In various other immunizing experiments active immunity was found likely to develop if the doses of antibody and virus were carefully graded by experiment.

He presumed that in the case of lambs receiving a dose of virus in experiment the large quantity of antibody present was out of all proportion to the amount of virus administered. In consequence no effect on the animals was observed; the antibody mechanism had not been stimulated to active production of antibodies. The titre of antibody remained as before administration of virus and subsequently fell at the same rate as in similarly immune lambs which had not received any virus.

AMERICAN SCHOLARSHIPS IN MEDICAL SCIENCE

The Markle Foundation (Fourteen Wall Street, New York 5, N.Y.) announce a new scholarship programme, to be undertaken in co-operation with the medical schools of the United States and Canada, for the purpose of relieving the teacher-investigator shortage in the schools. The announcement may be of special interest to some of our readers inasmuch as it includes a clause stating that persons engaged in work in the Associated Sciences might be considered.

The purpose of the programme is to attract much needed talent to academic medicine by giving promising young scientists academic security and financial assistance for a period up to five years. Grants of $25,000, payable to the co-operating school at the rate of $5,000 annually for a five-year period toward the support of each successful candidate or his research or both, will be available beginning with the academic year 1948-49. If the plan proves successful, the Foundation will appropriate a total of $1,250,000 to the schools by 1953.

Candidates will be recommended by medical schools and will be limited to young men and women with a particularly strong interest in research and teaching in any of the clinical or pre-clinical sciences or in the sciences basic to medicine. They will have had training in some special field or combination of fields to qualify them to receive a regular faculty appointment and to conduct original research. The final choice will be made, on the basis of the schools' recommendations, by regional committees appointed by the Foundation. The young scientists chosen will be known as "Scholars in Medical Science." No fixed number of scholars will be appointed in any year, but it is expected that approximately 50 will receive appointments during the five-year period. For each scholar, the school will determine salary and academic rank, encourage research by setting reasonable limits upon teaching and other non-research activities, provide laboratory facilities and, if necessary, make a financial contribution toward the support of his work.

The scholar programme places the emphasis on the personal qualities and scientific and teaching abilities of the men and women chosen, rather than upon particular research projects or teaching fields in which they may be interested. The programme is the result of a survey of medical research and education, recently made by the Foundation, which shows that while there are scholarships and other forms of financial aid for the student in the course of his scientific training and while there are funds available to the scientist once his name is made, there are few sources of help at the beginning of the career of the man who chooses academic medicine.

A pamphlet covering the details of the plan has been sent to all deans of accredited medical schools, and persons interested in being considered as candidates are referred to them for further information.

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Weekly Wisdom

Our vocabulary is already overburdened with American loans.—"The Times."

CLINICAL COMMUNICATION

The Use of 'Gammexane' in the Treatment of Sarcoptic Mange in Camels

By

MAJOR OMAR DRAZ, B.V.M.

Veterinary Section, Egyptian Army

Sarcoptic mange may be considered as one of the most important camel diseases in Egypt. M. S. Said (1946) reported that 75 per cent. of the 1,000 cases examined in the Cairo district were found to be infested by this disease: "a condition which has a serious economic effect on the working capacity of the animals, apart from the damage produced in the hides and the low quality of meat due to loss of condition in the diseased camel." According to this author the disease is caused by *Sarcoptes scabiei* var. *cameli* (Megnin, 1880), a parasite which is transmissible to human beings working with camels. No other form of mange in camels has been reported in Egypt.

Owing to the success achieved by the use of "Gammexane" products in controlling the camel tick, *Hyalomma aegyptium* (Lin., 1758), in a previous experiment carried out by the writer, it was thought that a successful treatment of camel mange with the same product would put an end to the two main troubles met by camel owners in this country.

During April, 1946, two camels were admitted to the Veterinary Hospital, E.A., Cairo, and both cases were clinically diagnosed as affected with sarcoptic mange. The lesions were widely spread over the head and neck, the shoulder region, chest, perineum, inside of the thighs and on the body. Scrapings were examined by Dr. Nagaty of the Parasitological Laboratory, Faculty of Medicine, Cairo, who confirmed the clinical diagnosis.

For treatment a sample of "Gammexane" liquid concentrate (L.G. 037) containing 7 per cent. of the gamma isomer of hexachlorocyclo-hexane was used. This was diluted in kerosene 1:13 to give a 0·5 per cent. "Gammexane" concentration. One camel was dressed by one litre of the diluted product. A piece of cloth was used in smearing every part of the body and rubbing well the affected parts. This was done in the early morning of May 2nd, 1946, and the camel was kept out of the hot sun. After a few minutes, symptoms of restlessness were observed. These faded gradually after a few hours. These symptoms are most probably caused by the irritation of the kerosene on the thick skin of the camel, or possibly the initial activity of the mange parasite in contact with the "Gammexane."

It was my intention to apply another dressing to this camel after 15 days but this was unnecessary owing to the disappearance of all clinical symptoms of mange. The skin was completely healthy and normal three weeks after the first and only dressing.

The second camel was kept as a control during the experiment. The lesions of mange spread over the other parts of the body. On June 6th, 1946, this camel was also dressed in a similar way and the same results were achieved.

Conclusion. The "Gammexane" product containing 0·5 per cent. of the gamma isomer 1 2 3 4 5 6 hexachlorocyclohexane in kerosene proved effective against *Sarcoptes scabiei* var. *cameli* (Megnin, 1880). The residual action of this product in the above-mentioned concentration was sufficient to give a complete cure after one dressing.

* * * *

'Gamatox' Fluid Dip

The above-mentioned results encouraged me to try "Gamatox" Fluid Dip containing "Gammexane" in the treatment of sarcoptic mange in camels.

Six camels, clinically showing symptoms of sarcoptic mange, were admitted to the Veterinary Hospital, E.A., Cairo. The diagnosis was confirmed microscopically in the same hospital. The disease was very advanced in two of the six camels.

Method.—The fluid was used at 1 part to 150 parts of water, giving an effective concentration of ·01 per cent. of the gamma isomer. No preliminary washing was carried out and the camels were not clipped before treatment. The fluid was sprayed on by means of a Hudson Sprayer, less than two gallons of fluid being found necessary for each camel. Five camels were sprayed and the sixth was kept as a control. Treatment was carried out four times at intervals of ten days between applications. The fluid was scrubbed well into the crusts and affected areas by means of a hard brush. The camels were groomed two days after each spraying.

Observations.—Itching and appearance of vesicles stopped in the first ten days, and during this period abrasions and even wounds

which were found in the two advanced cases, healed rapidly. The hair began to reappear after 20 days and after 30 days five cases were free of mange, while in the control case the disease was progressing rapidly over other parts of the body. The control camel was then treated in the same way and with the same results. As the experiment was made in January and February, 1947, which is not the season for the camel tick, *Hyalomma aegyptium*, no special consideration was given to tick counts, which will be done in the coming season. But it should be mentioned that it was very obvious that after this treatment ticks were reduced to a minimum.

Conclusions. "Gamatox" Fluid Dip at a strength to give ·01 per cent. of the gamma isomer, used as a spray four times at ten-day intervals, was found to be extremely effective as a treatment for sarcoptic mange in camels. It is considered possible that a smaller number of dressings might have effected a cure, but in the absence of exact knowledge regarding the life history of the sarcopt it was considered advisable to repeat treatment in the manner described.

Acknowledgment.—The writer is indebted to Messrs. Imperial Chemical Industries (Egypt), S.A., for the supply of the "Gammexane" L.G. 037 preparation and to Messrs. Cooper, McDougall & Robertson Ltd. for supplies of "Gamatox" Fluid Dip.

Reference

Said, M. S. (1946.) Ministry of Agriculture, Egypt, Technical and Scientific Service, Bull. No. 241, "Mange in Egyptian Camels."

ABSTRACTS

[Vaccination Studies on Bovine Trichomoniasis. Morgan, B. B. (1947.) *Amer. J. vet. Res.* **8**. 54-56.]

A review of the literature is given showing that earlier workers had succeeded in creating some measure of resistance against trichomoniasis by repeated intravenous or intramuscular injections of suspensions of *T. foetus*. The author describes an experiment designed to demonstrate the practical value of attempting to immunize heifers. Nine out of ten heifers were apparently protected temporarily against trichomoniasis by a series of 16 intramuscular or intravenous injections of living organisms at approximately semi-weekly intervals.

Seven out of ten animals after receiving six injections over a period of three weeks became infected with trichomoniasis. Two injections over a period of three weeks failed to protect eight out of ten heifers. Of the control group of heifers subjected to a similar measure of infection to the inoculated groups, only one become recognizably pregnant.

The author concludes that although temporary immunity may result after a long series of injections, the vaccination of heifers is ineffective for protecting breeding females and cannot be recommended as a practical procedure.

G. F. B.

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[Ketosis. Shaw, J. C. (1947.) *Univ. Penn. Bull., Vet. Ext. Quart.* No. 106. 41-48.]

This is a somewhat loosely written review of the whole subject of bovine ketosis. It is contended that ketosis in the recently calved dairy cow is due to the amount of blood sugar removed by the udder being greater than the body can replace. The glycogen stores in the liver become exhausted and the liver attempts to compensate for the lack of glycogen by using fat.

An incomplete review of the biochemical blood picture is given. Intravenous injections of carbohydrate are advocated as the best method of therapy.

Neither vitamin A nor massive doses of the vitamin B group proved of any value in treatment.

G. F. B.

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[The Diagnosis of Brucella Infection by means of a Rapid Agglutination Test with Blood or Milk from Cows. (Trans. title.) Thieulin, G., & Daspet, G. (1946.) *Bull. Acad. vét. France.* **19.** 299.]

The authors refer to the practical use of the rapid plate agglutination test in whole blood or milk for the detection of brucella infection in animals from infected herds, and the results are given in tabular form.

B. W.

REPORT

[Report on Animal Health and Husbandry in the Gold Coast, 1947. By Wm. C. Miller. Crown Agents for the Colonies, 4, Millbank, London, S.W.1. Price 2s.]

The object of Professor Miller's mission was the organization and administration of the Department of Animal Health of the Gold Coast and to make any necessary recommendations.

His report is worthy of study if only as a model of careful analysis, lucid description, moderate expression and dispassionate judgment.

In the course of his 24-day tour in November, 1945, Professor Miller travelled over 2,500 miles, often through the bush, inspected over 12,000 cattle at various centres and interviewed innumerable officers, chiefs and headmen.

The report begins with an excellent account of the general position of livestock in the Gold Coast, the various types of cattle and the system of management, which is interesting and informative. The much criticized cattle improvement scheme for the Northern Territories—native administrative farms—is then discussed, followed by details of the organization of the Animal Health Department. An outline of the general agricultural policy and the prospects for dairying complete a review from which the conclusions formed appear to be perfectly justified.

In view of the fact that the report clearly indicates friction between the Animal Health Department and the Agricultural Department it is not surprising that the final recommendations are mainly directed to its removal. They include the formation of a special Inter-Departmental Joint Standing Committee on Animal Husbandry under the chairmanship of the Colonial Secretary, the two departments concerned being represented by three senior members each, in order that future policy may be clearly defined and efficiently implemented by the allocation of specific responsibility to animal health and agricultural officers.

The remaining recommendations impress as being equally sound, although the suggestion that there should be two directors in the Animal Health Department (one of research and one of field services and administration) may not be universally accepted as workable in practice.

It is refreshing to read Professor Miller's carefully considered opinion that, despite a shortage of staff which was often serious, the Department of Animal Health has to its credit a record of achievement which will compare very favourably with the veterinary services in other colonial territories and which is far in excess of that shown by many.

Finally, it seems curious that although the tour was undertaken at the end of 1945 the report was not published until 1947.

G. B.

NOTES AND NEWS

Diary of Events

Oct. 14th.—Scientific Meeting of the Zoological Society of London, Regent's Park, N.W.8, 5 p.m.

Oct. 15th.—Meeting of the Section of Comparative Medicine, Royal Society of Medicine, 1, Wimpole Street, W.1, 5 p.m.

Oct. 15th.—Meeting of the South-Eastern Division, N.V.M.A., at Maidstone (Royal Star Hotel), 2.30 p.m.

Oct. 15th.—Meeting of the Midland Counties Division, N.V.M.A., at Newport, Salop (Harper Adams College), 2.30 p.m.

Oct. 16th.—Annual Meeting of the Central Veterinary Society, at the Royal Veterinary College, Camden Town, N.W.1, 2 p.m.

Oct. 22nd.—Special Meeting of Council, N.V.M.A., at the Connaught Rooms, Great Queen Street, Kingsway, London, W.C.2, 11.30 a.m.

Oct. 24th.—Autumn Meeting of the Eastern Counties Division, N.V.M.A., at Colchester (Red Lion Hotel), 2.15 p.m.

Oct. 24th.—Meeting of the Sussex Division, N.V.M.A., at Brighton (Old Ship Hotel), 2.30 p.m.

Oct. 29th.—Meeting of the Scottish Metropolitan Division, N.V.M.A., at the Royal "Dick" Veterinary College, Edinburgh, 2.30 p.m.

Oct. 30th.—Meeting of the Dumfries and Galloway Division, N.V.M.A., at Lockerbie (Lockerbie House Hotel), 2.15 p.m.

ROYAL SOCIETY OF MEDICINE

Section of Comparative Medicine

At a recent Council meeting of the above Section the office of President for 1947-48 was filled by the election of Mr. R. E. Glover, M.A., B.SC., F.R.C.V.S. As intimated in our Notices Columns, Mr. Glover will deliver his Presidential Address entitled "The influence of the small-animal breeder on biological research" at a meeting of the Section to be held at the Society's House, 1, Wimpole Street, London, W.1, on Wednesday, October 15th, at 5 p.m.

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PERSONAL

Appointment.—Dr. John F. A. Sprent, PH.D. (LOND.), B.SC. (ZOOL.) (LOND.), has accepted a position as senior research fellow in the department of parasitology of the Ontario Research Foundation, Toronto, Canada. He will be engaged in research on the pathology and immunology of helminth infections, particularly in wild animals. After a period as Veterinary Research Officer, Nigeria, Dr. Sprent has been working at the University of Chicago as a research fellow of the Veterinary Educational Trust and more recently has held the Seymour Coman Research Fellowship in parasitology at the University of Chicago.

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Births.—HAWKINS.—To Joy, wife of Derek Hawkins, B.SC., M.R.C.V.S., a daughter.

KERSHAW.—On September 20th, 1947, to Irene Margaret (*née* Jolliffe), wife of George Frederick Kershaw, a daughter—Susan.

NOEL.—On September 30th, 1947, to Doris (*née* Verrières), wife of Major E. Noel, a daughter.

TURNER.—To A. M. Turner, M.R.C.V.S. (*née* Abrams), wife of R. S. Turner, at the Barret Maternity Home, Northampton, a son—Michael.

WILSON.—At Glasgow, on September 28th, to the wife of John Edmund Wilson (Margaret B. Lennie, M.R.C.V.S.), Uisken Villa, East Bay, Dunoon, Argyllshire, a daughter.

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Marriages.—SMITH—GARDNER.—The wedding took place at the Congregational Church, Leamington Spa, on September 27th, 1947, between R. G. Smith, M.R.C.V.S., of Kilmarnock and Sandbank, and Lilian, daughter of Mrs. B. M. Gardner, Leamington Spa.

WILLIAMS—HARRIES.—On Thursday, September 4th, 1947, at Nantgaredig Methodist Chapel, Eric Idwal Williams, M.R.C.V.S., son of Mrs. Williams and the late Mr. J. T. Williams, The Grove, St. Clears, Carms., to Mary, daughter of Mrs. Harries and the late Mr. T. D. Harries, Penllwynan, Nantgaredig, Carms.

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R.C.V.S. OBITUARY

MAYALL, Gladstone, 24, Pool Street, Bolton. Graduated Glasgow, December 17th, 1895. Died October 3rd, 1947; aged 80 years.

SEWELL, Everard Dobbs, of The Square, and "Tapps," East Street, North Molton, Devon. Graduated London, December 11th, 1919. Died September 26th, 1947; aged 68 years.

Death of Mr. Gladstone Mayall, M.R.C.V.S.

The profession will learn with profound regret of the death of Gladstone Mayall, a well-loved member with deep practical knowledge of many aspects of its work.

Qualifying in Glasgow in 1895, Gladstone Mayall assisted Mr. Howes of Norwich. In 1910 he took over the extensive equine practice of James Bridge of Bolton, who became Bolton's first whole-time veterinary inspector. The practice included a busy forge employing at that time seven farriers, and the Corporation stud have been shod there ever since.

With the decline of the horse Gladstone Mayall turned his fertile brain to other matters, and was one of the first veterinarians seriously to study the diseases of poultry and feathered pets, and he was a regular contributor to poultry journals. Widely read and a deep thinker, his pen has been responsible for many articles in *The Veterinary Record*. His publications include "Cows, Cow-houses and Milk" and "Pigs, Pigsties and Pork." For many years he collaborated with the late Sir Frederick Hobday as Sub-Editor of *The Veterinary Journal*.

An accomplished linguist, speaking both French and German, his knowledge of the latter language was such as to enable him to undertake much of the translation of Hutyra and Marek's "Special Pathology," a work of great value to students and for reference.

His chief recreations were swimming and ballroom dancing, and up to the age of 75 he seldom missed a day without swimming several lengths in the Municipal Baths, while he was a well-known figure on many local dance floors.

His loss will be deeply mourned by his many colleagues in the profession, with whom his relations have always been most cordial, and in particular by the members of the Lancashire Division of which he was a past president, while he was ever a keen supporter and regular attender at meetings.

He leaves a widow and one daughter (Mrs. Trevor Potts), with whom much sympathy is felt in their bereavement.

Mr. E. D. Sewell, M.R.C.V.S.

Mr. Everard Sewell, whose death we record above with much regret, was widely known in agricultural and hunting circles in the South Molton area.

At North Molton he was a member of the Parish Council, and identified with a number of other local organizations. He had always taken a great interest in amateur dramatic art.

Mr. Sewell leaves a widow, who was his second wife.

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Veterinary Educational Trust

Wide Extension of Activities

On Tuesday last, *i.e.*, shortly before this issue went to press, announcement was made in the first full report of the Veterinary Educational Trust to be presented to the Annual Meeting of the Trustees and Council, of a greatly expanded programme of activities, the main features of which are a projected linked Research Station-County Hospital-Practitioner Service and a build-up of the Trust's machinery in the counties for the purpose of enlisting the active support of all livestock owners and all who appreciate the importance to the nation of a healthy animal population. A full notice of the report will appear in our next issue, reflecting its review of the successful foundation work which has now enabled the Trust confidently to undertake new enterprises. As our readers will be aware, these include the addition to its Equine and Canine Research Stations of a group of Farm Livestock Research Stations, while much interest attaches to the proposed development of a veterinary hospital service, working in full co-operation with practitioners and research workers.

To carry through its programme the Trust will require a minimum annual income of £20,000, and as a main means to the realization of this sum committees are to be established in each county, the objects of these County Committees being to further the interests of the Trust by securing financial support, by publicizing the aims and activities of the Trust, and generally by influencing public opinion in support of the promotion of animal health.

The new programme was the principal feature of the speeches at the luncheon which followed the Annual Meeting, when amongst those who promised the full support, in its fulfilment, of the bodies they represented were Sir Archibald Weigall (President, Royal Agricultural Society of England), Mr. Howard W. Dawes (President of the Royal College of Veterinary Surgeons) and Mr. L. Guy Anderson (President of the National Veterinary Medical Association). A report of this function will also appear next week.

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Veterinary Educational Trust Fellowship

Mr. T. K. Ewer, B.V.SC., H.D.A., has been awarded the B.O.C.M. Fellowship by the Veterinary Educational Trust. Work, in the first instance, will be concerned with the mineral and vitamin D metabolism of sheep. Mr. Ewer, when in New Zealand, made a field survey of sheep mortality in Canterbury and then continued his investigations and work on the spot. His main lines have been nutritional and parasitological. The Fellowship will be held at the Institute of Animal Pathology under the supervision of Professor Beveridge.

Mr. T. K. Ewer was born and educated in England and migrated to Australia when he was 17. He graduated at the Veterinary School at Sydney University in 1937.

In 1938 he went to New Zealand as a veterinary research officer in the Department of Agriculture. Some of his work done in New Zealand has been published in summarized form in the *New Zealand Journal of Agriculture* but the main part has not yet been published.

One aspect of the work in which Mr. Ewer is particularly interested is the relationship between rickets and the general unthrifti-

ness experienced during the animal's first winter and the composition of its diet.

He now wishes to investigate the mineral metabolism of growing sheep, with particular reference to the part played by phosphorus and vitamin D. In his investigations he hopes to use radio-active phosphorus. Such an investigation will be very useful not only in helping to clarify these problems in New Zealand but also similar or related problems in this country.

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Professor Telesforo Bonadonna of the University of Milan, Director of the Experimental Institute for Artificial Insemination, has been appointed Chairman of the "Societa Italiana per il Progresso Della Zootecnica" (Italian Association for the Progress of Zootechny). This Association was established at Milan on July 17th, 1947, to encourage by all possible means zootechnical progress in that country, and to keep in close technical collaboration with zootechnical and veterinary institutions throughout the world.

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Scheme for the Control of Diseases of Dairy Cattle

STATEMENT SHOWING THE NUMBER OF UNDERTAKINGS NOTIFIED TO THE MINISTRY OF AGRICULTURE DURING THE MONTH ENDED SEPTEMBER 30TH, 1947

County	Undertakings Notified		Total Undertakings		
	During Month	Previously	Number	Number of Cattle	
				Cows	Heifers
ENGLAND					
Bedford	—	8	8	145	77
Berks	1	46	47	1,516	1,052
Bucks	—	22	22	561	569
Cambridge	—	—	—	—	—
Cheshire	2	133	135	4,567	1,976
Cornwall	—	—	—	—	—
Cumberland	—	9	9	387	304
Derby	5	213	218	6,200	3,485
Devon	1	115	116	1,703	1,244
Dorset	—	11	11	352	147
Durham	3	157	160	3,431	1,431
Essex	—	95	95	3,290	2,491
Gloucester	—	31	31	1,057	871
Hampshire	5	117	122	4,166	2,716
Hereford	—	5	5	163	137
Hertford	—	26	26	867	555
Hunts	—	—	—	—	—
Isle of Ely	—	—	—	—	—
Isle of Wight	—	—	—	—	—
Kent	2	70	72	1,579	1,095
Lancs	1	82	83	2,524	1,137
Leics	1	59	60	1,492	1,237
Lincs (Holland)	—	—	—	—	—
Lincs (Kesteven)	—	13	13	172	141
Lincs (Lindsay)	1	12	13	388	401
Middlesex	—	2	2	34	25
Norfolk	—	51	51	1,585	1,202
Northants	1	20	21	513	568
Northumberland	2	31	33	1,075	769
Notts	2	105	107	2,581	1,438
Oxford	2	8	10	270	224
Rutland	—	—	—	—	—
Salop	1	57	58	7,930	1,141
Soke of Peterborough	—	—	—	—	—
Somerset	—	100	100	2,461	1,464
Staffs	4	90	94	2,772	1,866
Suffolk (East)	—	22	22	435	327
Suffolk (West)	—	25	25	497	414
Surrey	1	46	47	1,264	780
Sussex (East)	—	59	59	1,790	1,260
Sussex (West)	—	35	35	1,143	704
Warwick	4	61	65	1,740	1,089
Westmorland	—	3	3	51	21
Wilts	—	35	35	1,365	906
Worcester	1	77	78	1,490	868
Yorks (E.R.)	2	44	46	758	577
Yorks (N.R.)	—	55	55	1,248	869
Yorks (W.R.)	1	106	107	2,598	1,280
WALES					
Anglesey	1	9	10	151	109
Brecon	—	5	5	99	68
Caernarvon	—	26	26	480	209
Cardigan	—	29	29	599	406
Carmarthen	—	145	145	2,856	1,540
Denbigh	—	11	11	215	111
Flint	—	23	23	576	274
Glamorgan	—	33	33	535	300
Merioneth	—	6	6	93	31
Monmouth	—	8	8	165	123
Montgomery	—	—	—	—	—
Pembroke	—	7	7	197	235
Radnor	—	—	—	—	—
TOTALS	44	2,558	2,602	74,226	42,264
SCOTLAND					
Aberdeen	—	17	17	913	398
Angus	—	13	13	540	345
Argyll	—	—	—	—	—
Ayr	—	10	10	350	222
Banff	—	1	1	120	20
Berwick	—	1	1	22	7
Bute	—	—	—	—	—
Caithness	—	—	—	—	—
Clackmannan	—	1	1	19	14
Dumfries	—	12	12	617	564
Dunbarton	—	—	—	—	—
East Lothian	—	1	1	20	8
Fife	—	23	23	708	498
Inverness	—	—	—	—	—
Kincardine	—	2	2	60	68
Kinross	—	3	3	60	43
Kirkcudbright	—	6	6	781	712
Lanark	—	5	5	235	150
Midlothian	—	—	—	—	—
Moray	—	—	—	—	—
Nairn	—	—	—	—	—
Orkney	—	—	—	—	—
Peebles	—	—	—	—	—
Perth	—	12	12	412	292
Renfrew	—	4	4	151	101
Ross-shire	—	3	3	130	62
Roxburgh	—	—	—	—	—
Selkirk	—	—	—	—	—
Stirling	—	7	7	254	219
Sutherland	—	4	4	85	39
West Lothian	1	2	3	95	53
Wigtown	—	15	15	1,247	708
Zetland	—	—	—	—	—
TOTALS	1	142	143	6,819	4,523

Notes.—(1) Operative periods of undertakings: 1 year, 697; 2 years, 149; 3 years, 1,756. (2) Undertakings renewed for further periods: 1 year, 14; 2 years, 1; 3 years, 1. (3) Undertakings not renewed at end of operative periods, 71. (4) The figures showing the number of undertakings notified during the month relate to entirely fresh undertakings and do not include undertakings renewed for further periods. Undertakings which have been cancelled or not renewed are not included in the figures for previous notifications.

Notes.—(1) Duration of undertakings: 1 year, 44; 2 years, 5; 3 years, 94. (2) Undertakings renewed for a further period (included in column 2 of statement): 1 year, 125; 2 years, 9; 3 years, 72. (3) Undertakings expired and not renewed (not included in column 2 of statement), 260. (4) The figures in the first column of the statement relate to entirely fresh undertakings.

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First Graduation of Africans Trained as Veterinarians in Nigeria

LANDMARK IN COLONIAL VETERINARY DEVELOPMENT

The *Nigeria Review* records that a ceremony unique in the history of Nigeria took place recently at the Veterinary Department's Headquarters at Vom, to mark the graduation of Mr. T. A. Mbaeliachi and Mr. W. O. Ndep as the first two veterinarians to be trained in the country. We learn that both have been accepted into the Veterinary Service of the Nigerian Government as Assistant Veterinary Officers.

The ceremony was opened by Mr. W. G. Beaton, Acting Director of Veterinary Services, who said: "We have come here to-day to witness a ceremony which is unique in the history of Nigeria but one which we hope will become a regular event in the future, and it is the graduation of Africans trained as Veterinarians in Nigeria.

"The Veterinary School at Vom, long the dream of very many of us, was commenced in the early part of the war. It had its foundation stone laid in 1943 and was completed about 1946 at a total cost of £51,000, paid from the Colonial Development Fund. Due to the war, naturally the scheme passed through a great many vicissitudes but these were all surmounted in the end and I should like now to pay tribute particularly to the late Director of Veterinary Services, Captain W. W. Henderson, C.B.E., whose driving force and determination saw this scheme put through from its conception until almost the completion. I feel sure that Captain Henderson would have liked to have been amongst us to-day and I am sure we would all have wished it also.

"Although we have passed out from this School quite a number of Africans trained as Senior Veterinary Assistants and Junior Veterinary Assistants, to-day is really the first harvest of the scheme, namely, the graduation, the completion of the training, of fully-trained veterinarians and this of course fits in with the general policy for the higher education of the African. It is a proud moment for all of us who have been concerned in it."

Mr. Beaton concluded by welcoming Sir John Patterson, K.B.E., C.M.G., Chief Commissioner, Northern Provinces, and Lady Patterson.

Sir John Patterson said that he counted it a privilege to share in the pleasure of the Director and his staff in what he knew was the culmination of a desire of many years and the consummation of an effort that had not been easy. He told the two men that they were going out to undertake extremely important work at a very critical time in the country's history. They were a small army against large forces.

BAN ON THE IMPORT OF BOOKS

Our own comments last week on the above measure are forcefully supplemented by the following editorial note in the issue of *Nature* of October 4th.

As one of the measures for reducing British expenditure in countries in the "dollar area," it has been announced that restrictions are being imposed on the importation into Britain of books. At a time when emphasis is being placed increasingly on the importance of international understanding, it is most unfortunate that this particular medium should have been selected as a means of effecting economies; books are surely one of the best means of making one people acquainted with another. Here we are concerned mainly with scientific and technical books, and the restriction will in practice apply chiefly, though not entirely, to American books. The position is that scientific and technical books may no longer be imported except under individual licence. British publishers have to submit to the licensing authorities evidence of the value of their pre-war imports of such books, and they will be given a licence to import foreign books to the same annual value. Thus we return, at a stroke, to the maximum war-time restrictions. Publishers will now have to apply quarterly for licences to import specified quantities of named books, and giving in each case the name of the exporting country.

There are some observations on such a scheme which immediately come to mind. First there is the vexatious delay in obtaining a necessary book, should the British publisher have no copy in stock. Further, in imposing this form of individual licence, the Government is in effect instituting a system which might easily become a form of censorship. A more immediate objection is that the present scheme is based on money value, and takes no account of the increase in book production costs. So far as American books are concerned, prices are 50 per cent. and more above the pre-war figure for corresponding books. In effect, therefore, the number of scientific and technical books of American origin it will be possible to import into Britain will be substantially less than the figure for 1939.

It is becoming generally accepted that the utmost efficiency is necessary in the scientific and technical fields to enable Britain to recover its position in the world. Yet by cutting down supplies of the essential books, the Government is putting an important obstacle in the path; and this at a time when there is an acute shortage of school and university text-books and also of standard works of reference. It may be urged that some American text-books are not suited for the courses in British schools and universities, but that argument cannot be applied to research monographs and reference works; these, with the all-important specialist periodicals, are essential tools for the scientific worker trying to keep abreast of modern developments.

While it must be granted that restrictions on general expenditure are necessary, it would seem that scientific and technical books should have a high priority in the permissible expenditure of dollars; and it should be possible to devise a scheme whereby such books are made more readily available.

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FOWL PEST IN NORFOLK

In a notification which was received too late for inclusion in our last issue, the Ministry of Agriculture and Fisheries states that there has recently been a sharp increase in the incidence of fowl pest in Norfolk, where 40 outbreaks were confirmed during September. The movement of birds from that county has been responsible for setting up the disease in other parts of the country. Because of this danger to the health of poultry flocks in Norfolk and elsewhere, the Minister of Agriculture and Fisheries has made an Order (The Norfolk Sales, Exhibitions and Collection of Live Poultry (Prohibition) Order of 1947) which has the effect of prohibiting in Norfolk the sale or exhibition of poultry (other than day-old chicks) and the collection of such poultry in that county by dealers. The Order does not prevent the sale of poultry stock by a poultry-keeper direct from his premises so long as he has not, within 28 days preceding the sale, brought any poultry on to those premises.

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The Canadian Department of Agriculture have announced that cattle, sheep, goats and swine may now be imported into Canada from Scotland in view of the fact that there has been no outbreak of foot-and-mouth disease in Scotland since early this year. Shipments must come direct from a Scottish port, animals must have been in Scotland for 60 days prior to embarkation and feeding-stuffs used on the voyage must have been grown in Scotland.

CORRESPONDENCE

The views expressed in letters addressed to the Editor represent the personal opinions of the writer only and their publication does not imply endorsement by the N.V.M.A.

Correspondents should write as briefly as possible and letters should not exceed 350 words.

PREGNANCY DIAGNOSIS BY PALPATION OF THE FOETAL MEMBRANES

Sir,—I was amused to read that the old controversy over pregnancy diagnosis by palpation of the foetal membranes had arisen once again.

Mr. Steele-Bodger, in his letter published in your issue of September 27th, states that, generally speaking, at three to three and a half months he would find it quite impossible to pick up a fold of the gravid uterus, and that palpation of foetal membranes is the most unreliable of all methods of distinction between pregnancy and pyometra.

The American clinician, M. G. Fincher, in a paper entitled "Some Phases of Sterility in Cattle" read at the 33rd annual conference for veterinarians at Cornell, 1941, writes as follows when discussing pregnancy diagnosis:—

"Palpation of the uterus at 38 to 90 days will reveal one horn larger than the other and both will usually be filled with fluid under tension. The fetal membranes may be felt to be sure one is not dealing with pyometra or hydrometra, or mucometra. The method suggested by Danelius of Linkoping, Sweden, and shown by Gotze in his film in 1938 at the International Veterinary Congress, consists of picking up the uterus and its fetal membranes first allowing the fetal membranes to slip between the thumb and index or other finger. Then the uterus, or dorsal uterine wall will be felt to slip between the finger and thumb. If there is but one tissue to slip, it will be the uterine wall, and it means that the uterus does not contain normal fetal sacs. The middle, or the third fingers have proved to me to be the ones that most easily pick up the uterus and chorion. *This simple and infallible test is most easily used at* 40 *to* 95 *days of pregnancy* (my italics). It should preferably not be used before 40 days of pregnancy, but is *extremely accurate* in the dairy cow as early as 40 days of pregnancy. It is more difficult to apply to fat heifers than to older cows. The membrane test is especially easy to apply at the middle or near the apex of the gravid uterine horn. One slip of the membrane is all that is needed and takes less time than to make other tests for pregnancy."

Contrary to Mr. Steele-Bodger's contention that it is almost impossible to carry out this technique at three to three and a half months, Fincher declares that at 40 to 95 days it is both simple and infallible.

Somebody must be wrong!

Yours faithfully,

L. E. Rowson, M.R.C.V.S.,
Director,
Cambridge & District Cattle Breeders Ltd.

The Gravel Pits,
Huntingdon Road,
Cambridge.

September 30th, 1947.

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ASCERTAINING "REPRESENTATIVE" OPINION

Sir,—Letters in these columns under the heading "Ascertaining 'Representative' Opinion" seem to be well off the subject now; perhaps I am partly to blame.

Your correspondent, Mr. Tutt, however, is to be congratulated on his views as regards assistants. They appear almost philanthropical compared with the ideas of others.

I would like to mention in passing, however, that he rather missed the point in reference to myself. I have always been in general practice—except for a vacation in H.M. Forces—and as a partner in a well-established practice already occupy the post he advises me to assume. Moreover, I have no desire whatsoever to revert to the position of an employee.

It looks as if "the agitator" is a person living in a glass house who has had the temerity to throw stones.

Yours faithfully,

John D. Parkinson.

"Norlands,"
Bainbridge Road,
Sedbergh.

October 5th, 1947.